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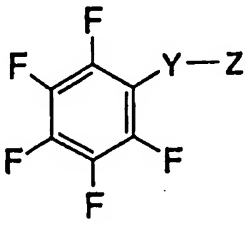
(57) Abstract

The invention provides methods and compositions relating to novel pentafluorophenylsulfonamide derivatives and analogs and their use as pharmacologically active agents. The compositions find particular use as pharmacological agents in the treatment of disease states, particularly cancer, vascular restenosis, microbial infections, and psoriasis, or as lead compounds for the development of such agents. The compositions include compounds of general formula (I).



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Pentafluorobenzenesulfonamides and Analogs

INTRODUCTION

Field of the Invention

The field of the invention is pentafluorobenzenesulfonamide derivatives and analogs and their use as pharmacologically active agents.

Background

A number of human diseases stem from processes of uncontrolled or abnormal cellular proliferation. Most prevalent among these is cancer, a generic name for a wide range of cellular malignancies characterized by unregulated growth, lack of differentiation, and the ability to invade local tissues and metastasize. These neoplastic malignancies affect, with various degrees of prevalence, every tissue and organ in the body. A multitude of therapeutic agents have been developed over the past few decades for the treatment of various types of cancer. The most commonly used types of anticancer agents include: DNA-alkylating agents (e.g., cyclophosphamide, ifosfamide), antimetabolites (e.g., methotrexate, a folate antagonist, and 5-fluorouracil, a pyrimidine antagonist), microtubule disruptors (e.g., vincristine, vinblastine, paclitaxel), DNA intercalators (e.g., doxorubicin, daunomycin, cisplatin), and hormone therapy (e.g., tamoxifen, flutamide). The ideal antineoplastic drug would kill cancer cells selectively, with a wide therapeutic index relative to its toxicity towards non-malignant cells. It would also retain its efficacy against malignant cells even after prolonged exposure to the drug. Unfortunately, none of the current chemotherapies possess an ideal profile. Most possess very narrow therapeutic indexes, and in practically every instance cancerous cells exposed to slightly sublethal concentrations of a chemotherapeutic agent will develop resistance to such an agent, and quite often cross-resistance to several other antineoplastic agents.

Psoriasis, a common chronic skin disease characterized by the presence of dry scales and plaques, is generally thought to be the result of abnormal cell proliferation. The disease results from hyperproliferation of the epidermis and incomplete differentiation of keratinocytes. Psoriasis often involves the scalp, elbows, knees, back, buttocks, nails, eyebrows, and genital

regions, and may range in severity from mild to extremely debilitating, resulting in psoriatic arthritis, pustular psoriasis, and exfoliative psoriatic dermatitis. No therapeutic cure exists for psoriasis. Milder cases are often treated with topical corticosteroids, but more severe cases may be treated with antiproliferative agents, such as the antimetabolite methotrexate, the DNA synthesis inhibitor hydroxyurea, and the microtubule disrupter colchicine.

Other diseases associated with an abnormally high level of cellular proliferation include restenosis, where vascular smooth muscle cells are involved, inflammatory disease states, where endothelial cells, inflammatory cells and glomerular cells are involved, myocardial infarction, where heart muscle cells are involved, glomerular nephritis, where kidney cells are involved, transplant rejection, where endothelial cells are involved, infectious diseases such as HIV infection and malaria, where certain immune cells and/or other infected cells are involved, and the like. Infectious and parasitic agents per se (e.g. bacteria, trypanosomes, fungi, etc) are also subject to selective proliferative control using the subject compositions and compounds.

Accordingly, it is one object of the present invention to provide compounds which directly or indirectly are toxic to actively dividing cells and are useful in the treatment of cancer, viral and bacterial infections, vascular restenosis, inflammatory diseases, autoimmune diseases, and psoriasis.

A further object of the present invention is to provide therapeutic compositions for treating said conditions.

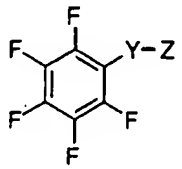
Still further objects are to provide methods for killing actively proliferating cells, such as cancerous, bacterial, or epithelial cells, and treating all types of cancers, infections, inflammatory, and generally proliferative conditions. A further object is to provide methods for treating other medical conditions characterized by the presence of rapidly proliferating cells, such as psoriasis and other skin disorders.

Other objects, features and advantages will become apparent to those skilled in the art from the following description and claims.

SUMMARY OF THE INVENTION

The invention provides methods and compositions relating to novel pentafluorophenylsulfonamide derivatives and analogs and their use as pharmacologically active agents. The compositions find particular use as pharmacological agents in the treatment of disease states, particularly cancer, bacterial infections and psoriasis, or as lead compounds for the development of such agents.

In one embodiment, the invention provides for the pharmaceutical use of compounds of the general formula I and for pharmaceutically acceptable compositions of compounds of formula I:



I

or a physiologically acceptable salt thereof, wherein:

Y is -S(O)- or -$S(O)_2$-;

Z is -NR^1R^2 or -OR^3, where R^1 and R^2 are independently selected from

hydrogen,

substituted or unsubstituted (C1-C10)alkyl,

substituted or unsubstituted (C1-C10)alkoxy,

substituted or unsubstituted (C3-C6)alkenyl,

substituted or unsubstituted (C2-C6)heteroalkyl,

substituted or unsubstituted (C3-C6)heteroalkenyl,

substituted or unsubstituted (C3-C6)alkynyl,

substituted or unsubstituted (C3-C8)cycloalkyl,

substituted or unsubstituted (C5-C7)cycloalkenyl,

substituted or unsubstituted (C5-C7)cycloalkadienyl,

substituted or unsubstituted aryl,

substituted or unsubstituted aryloxy,

substituted or unsubstituted aryl-(C3-C8)cycloalkyl,

substituted or unsubstituted aryl-(C5-C7)cycloalkenyl,

substituted or unsubstituted aryloxy-(C3-C8)cycloalkyl,

substituted or unsubstituted aryl-(C1-C4)alkyl,
substituted or unsubstituted aryl-(C1-C4)alkoxy,
substituted or unsubstituted aryl-(C1-C4)heteroalkyl,
substituted or unsubstituted aryl-(C3-C6)alkenyl,
substituted or unsubstituted aryloxy-(C1-C4)alkyl,
substituted or unsubstituted aryloxy-(C2-C4)heteroalkyl,
substituted or unsubstituted heteroaryl,
substituted or unsubstituted heteroaryloxy,
substituted or unsubstituted heteroaryl-(C1-C4)alkyl,
substituted or unsubstituted heteroaryl-(C1-C4)alkoxy,
substituted or unsubstituted heteroaryl-(C1-C4)heteroalkyl,
substituted or unsubstituted heteroaryl-(C3-C6)alkenyl,
substituted or unsubstituted heteroaryloxy-(C1-C4)alkyl, and
substituted or unsubstituted heteroaryloxy-(C2-C4)heteroalkyl,

wherein R^1 and R^2 may be connected by a linking group E to give a substituent of the formula

wherein E represents a bond, (C1-C4) alkylene, or (C1-C4) heteroalkylene, and the ring formed by R^1, E, R^2 and the nitrogen contains no more than 8 atoms. or preferably the R^1 and R^2 may be covalently joined in a moiety that forms a 5- or 6-membered heterocyclic ring with the nitrogen atom of NR^1R^2;

and where R^3 is a substituted or unsubstituted aryl or heteroaryl group.

Substituents for the alkyl, alkoxy, alkenyl, heteroalkyl, heteroalkenyl, alkynyl, cycloalkyl, heterocycloalkyl, cycloalkenyl, and cycloalkadienyl radicals are selected independently from

-H
-OH
-O-(C1-C10)alkyl
=O
$-NH_2$

-NH-(C1-C10)alkyl

-N[(C1-C10)alkyl]$_2$

-SH

-S-(C1-C10)alkyl

-halo

-Si[(C1-C10)alkyl]$_3$

in a number ranging from zero to (2N+1), where N is the total number of carbon atoms in such radical.

Substituents for the aryl and heteroaryl groups are selected independently from

-halo

-OH

-O-R'

-O-C(O)-R'

-NH_2

-NHR'

-NR'R"

-SH

-SR'

-R'

-CN

-NO_2

-CO_2H

-CO_2-R'

-$CONH_2$

-CONH-R'

-CONR'R"

-O-C(O)-NH-R'

-O-C(O)-NR'R"

-NH-C(O)-R'

-NR"-C(O)-R'

-NH-C(O)-OR'

-NR"-C(O)-R'

-NH-C(NH_2)=NH

-NR'-C(NH_2)=NH

-NH-C(NH_2)=NR'

-S(O)-R'

-$S(O)_2$-R'

-$S(O)_2$-NH-R'

-$S(O)_2$-NR'R"

-N_3

-$CH(Ph)_2$

substituted or unsubstituted aryloxy

substituted or unsubstituted arylamino

substituted or unsubstituted heteroarylamino

substituted or unsubstituted heteroaryloxy

substituted or unsubstituted aryl-(C1-C4)alkoxy,

substituted or unsubstituted heteroaryl-(C1-C4)alkoxy,

perfluoro(C1-C4)alkoxy, and

perfluoro(C1-C4)alkyl,

in a number ranging from zero to the total number of open valences on the aromatic ring system;

and where R' and R" are independently selected from :

substituted or unsubstituted (C1-C10)alkyl,

substituted or unsubstituted (C1-C10)heteroalkyl,

substituted or unsubstituted (C2-C6)alkenyl,

substituted or unsubstituted (C2-C6)heteroalkenyl,

substituted or unsubstituted (C2-C6)alkynyl,

substituted or unsubstituted (C3-C8)cycloalkyl,

substituted or unsubstituted (C3-C8)heterocycloalkyl,

substituted or unsubstituted (C5-C6)cycloalkenyl,

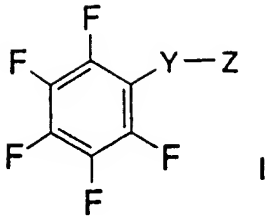
substituted or unsubstituted (C5-C6)cycloalkadienyl,

substituted or unsubstituted aryl,
substituted or unsubstituted aryl-(C1-C4)alkyl,
substituted or unsubstituted aryl-(C1-C4)heteroalkyl,
substituted or unsubstituted aryl-(C2-C6)alkenyl,
substituted or unsubstituted aryloxy-(C1-C4)alkyl,
substituted or unsubstituted aryloxy-(C1-C4)heteroalkyl,
substituted or unsubstituted heteroaryl,
substituted or unsubstituted heteroaryl-(C1-C4)alkyl,
substituted or unsubstituted heteroaryl-(C1-C4)heteroalkyl,
substituted or unsubstituted heteroaryl-(C2-C6)alkenyl,
substituted or unsubstituted heteroaryloxy-(C1-C4)alkyl, and
substituted or unsubstituted heteroaryloxy-(C1-C4)heteroalkyl.

Two of the substituents on adjacent atoms of the aryl or heteroaryl ring may optionally be replaced with a substituent of the formula -T-C(O)-$(CH_2)_n$-U-, wherein T and U are independently selected from N, O, and C, and n = 0-2. Alternatively, two of the substituents on adjacent atoms of the aryl or heteroaryl ring may optionally be replaced with a substituent of the formula -A-(CH2)p-B-, wherein A and B are independently selected from C, O, N, S, SO, SO_2, and SO_2NR', and p = 1-3. One of the single bonds of the new ring so formed may optionally be replaced with a double bond. Alternatively, two of the substituents on adjacent atoms of the aryl or heteroaryl ring may optionally be replaced with a substituent of the formula -$(CH_2)_q$-X-$(CH_2)_r$-, where q and r are independently 1-3, and X is selected from O, N, S, SO, SO_2 and SO_2NR'. The substituent R' in SO_2NR' is selected from hydrogen or (C1-C6)alkyl.

In another embodiment, the invention provides novel methods for the use of pharmaceutical compositions containing compounds of the foregoing description of the general formula I. The invention provides novel methods for treating pathology such as cancer, bacterial infections and psoriasis, including administering to a patient an effective formulation of one or more of the subject compositions.

In another embodiment, the invention provides chemically-stable, pharmacologically active compounds of general formula I:



I

or a pharmaceutically acceptable salt thereof, wherein:

Y is -S(O)- or -S(O_2)-; and

Z is NR^1R^2, wherein R^2 is an optionally substituted aryl or heteroaryl group, and R^1 is selected from:

hydrogen,

substituted or unsubstituted (C1-C10)alkyl,

substituted or unsubstituted (C1-C10)alkoxy,

substituted or unsubstituted (C3-C6)alkenyl,

substituted or unsubstituted (C2-C6)heteroalkyl,

substituted or unsubstituted (C3-C6)heteroalkenyl,

substituted or unsubstituted (C3-C6)alkynyl,

substituted or unsubstituted (C3-C8)cycloalkyl,

substituted or unsubstituted (C5-C7)cycloalkenyl,

substituted or unsubstituted (C5-C7)cycloalkadienyl,

substituted or unsubstituted aryl,

substituted or unsubstituted aryloxy,

substituted or unsubstituted aryl-(C3-C8)cycloalkyl,

substituted or unsubstituted aryl-(C5-C7)cycloalkenyl,

substituted or unsubstituted aryloxy-(C3-C8)cycloalkyl,

substituted or unsubstituted aryl-(C1-C4)alkyl,

substituted or unsubstituted aryl-(C1-C4)alkoxy,

substituted or unsubstituted aryl-(C1-C4)heteroalkyl,

substituted or unsubstituted aryl-(C3-C6)alkenyl,

substituted or unsubstituted aryloxy-(C1-C4)alkyl,

substituted or unsubstituted aryloxy-(C2-C4)heteroalkyl,

substituted or unsubstituted heteroaryl,

substituted or unsubstituted heteroaryloxy,

substituted or unsubstituted heteroaryl-(C1-C4)alkyl,

substituted or unsubstituted heteroaryl-(C1-C4)alkoxy,

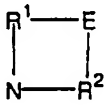
substituted or unsubstituted heteroaryl-(C1-C4)heteroalkyl,

substituted or unsubstituted heteroaryl-(C3-C6)alkenyl,

substituted or unsubstituted heteroaryloxy-(C1-C4)alkyl, and

substituted or unsubstituted heteroaryloxy-(C2-C4)heteroalkyl,

wherein R^1 and R^2 may be connected by a linking group E to give a substituent of the formula



wherein E represents a bond, (C1-C4) alkylene, or (C1-C4) heteroalkylene, and the ring formed by R^1, E, R^2 and the nitrogen contains no more than 8 atoms, or preferably the R^1 and R^2 may be covalently joined in a moiety that forms a 5- or 6-membered heterocyclic ring with the nitrogen atom of NR^1R^2;

provided that:

in the case that Y is $-S(O_2)-$, and R^1 is hydrogen or methyl, then R^2 is substituted phenyl or heteroaryl group;

in the case that Y is $-S(O_2)-$ and R^2 is a ring system chosen from 1-naphthyl, 5-quinolyl, or 4-pyridyl, then either R^1 is not hydrogen or R^2 is substituted by at least one substituent that is not hydrogen;

in the case that Y is $-S(O_2)-$, R^2 is phenyl, and R^1 is a propylene unit attaching the nitrogen of $-NR^1R^2-$ to the 2- position of the phenyl ring in relation to the sulfonamido group to form a 1,2,3,4-tetrahydroquinoline system, one or more of the remaining valences on the bicyclic system so formed is substituted with at least one substituent that is not hydrogen;

in the case that Y is $-S(O_2)-$ and R^2 is phenyl substituted with 3-(1-hydroxyethyl), 3-dimethylamino, 4-dimethylamino, 4-phenyl, 3-hydroxy, 3-hydroxy-4-diethylaminomethyl, 3,4-methylenedioxy, 3,4-ethylenedioxy, 2-(1-pyrrolyl), or 2-methoxy-4-(1-morpholino), then either R^1 is not hydrogen or when R^1 is hydrogen, one or more of the remaining valences on the phenyl ring of R^2 is substituted with a substituent that is not hydrogen;

in the case that Y is $-S(O_2)-$ and R^2 is 2-methylbenzothiazol-5-yl,

6-hydroxy-4-methyl-pyrimidin-2-yl, 3-carbomethoxypyrazin-2-yl, 5-carbomethoxypyrazin-2-yl, 4-carboethoxy-1-phenylpyrazol-5-yl, 3-methylpyrazol-5-yl, 4-chloro-2-methylthiopyrimidin-6-yl, 2-trifluoromethyl-1,3,4-thiadiazol-5-yl, 5,6,7,8-tetrahydro-2-naphthyl, 4-methylthiazol-2-yl, 6,7-dihydroindan-5-yl, 7-chloro-5-methyl-1,8-naphthyridin-2-yl, 5,7-dimethyl-1,8-naphthyridin-2-yl, or 3-cyanopyrazol-4-yl, R^1 is a group other than hydrogen.

DETAILED DESCRIPTION OF THE INVENTION

The term "alkyl" by itself or as part of another substituent means, unless otherwise stated, a straight or branched chain hydrocarbon radical, including di- and multi-radicals, having the number of carbon atoms designated (i.e. C1-C10 means one to ten carbons) and includes straight or branched chain groups such as methyl, ethyl, n-propyl, isopropyl, n-butyl, t-butyl, isobutyl, sec-butyl, homologs and isomers of n-pentyl, n-hexyl, 2-methylpentyl, 1,5-dimethylhexyl, 1-methyl-4-isopropylhexyl and the like. The term "alkylene" by itself or as part of another substituent means a divalent radical derived from an alkane, as exemplified by $-CH_2CH_2CH_2CH_2-$. A "lower alkyl" is a shorter chain alkyl, generally having six or fewer carbon atoms.

The term "heteroalkyl" by itself or in combination with another term means, unless otherwise stated, a stable straight or branched chain radical consisting of the stated number of carbon atoms and one or two heteroatoms selected from the group consisting of O, N, and S, and wherein the nitrogen and sulfur atoms may optionally be oxidized and the nitrogen heteroatom may optionally be quaternized. The heteroatom(s) may be placed at any position of the heteroalkyl group, including between the rest of the heteroalkyl group and the fragment to which it is attached, as well as attached to the most distal carbon atom in the heteroalkyl group. Examples include $-O-CH_2-CH_2-CH_3$, $-CH_2-CH_2-O-CH_3$, $-CH_2-CH_2-CH_2-OH$, $-CH_2-CH_2-NH-CH_3$, $-CH_2-CH_2-N(CH_3)-CH_3$, $-CH_2-S-CH_2-CH_3$, $-CH_2-CH_2-S(O)-CH_3$, $-O-CH_2-CH_2-CH_2-NH-CH_3$, and $-CH_2-CH_2-S(O)_2-CH_3$. Up to two heteroatoms may be consecutive, such as, for example, $-CH_2-NH-OCH_3$. The term "heteroalkylene" by itself or as part of another substituent means a divalent radical derived from heteroalkyl, as exemplified by $-CH_2-CH_2-S-CH_2-CH_2-$ and $-CH_2-S-CH_2-CH_2-NH-$.

The terms "cycloalkyl" and "heterocycloalkyl", by themselves or in combination with

other terms, represent, unless otherwise stated, cyclic versions of "alkyl" and "heteroalkyl", respectively. Examples of cycloalkyl include cyclopentyl, cyclohexyl, cycloheptyl, and the like. Examples of heterocycloalkyl include 1-piperidinyl, 2-piperidinyl, 3-piperidinyl, 4-morpholinyl, 3-morpholinyl, tetrahydrofuran-2-yl, tetrahydrofuran-3-yl, tetrahydrothien-2-yl, tetrahydrothien-3-yl, 1-piperazinyl, 2-piperazinyl, and the like.

The term "alkenyl" employed alone or in combination with other terms, means, unless otherwise stated, a stable straight chain or branched monounsaturated or diunsaturated hydrocarbon group having the stated number of carbon atoms. Examples include vinyl, propenyl (allyl), crotyl, isopentenyl, butadienyl, 1,3-pentadienyl, 1,4-pentadienyl, and the higher homologs and isomers. A divalent radical derived from an alkene is exemplified by $-CH=CH-CH_2-$.

The term "heteroalkenyl" by itself or in combination with another term means, unless otherwise stated, a stable straight or branched chain monounsaturated or diunsaturated hydrocarbon radical consisting of the stated number of carbon atoms and one or two heteroatoms selected from the group consisting of O, N, and S, and wherein the nitrogen and sulfur atoms may optionally be oxidized and the nitrogen heteroatom may optionally be quarternized. Up to two heteroatoms may be placed consecutively. Examples include $-CH=CH-O-CH_3$, $-CH=CH-CH_2-OH$, $-CH_2-CH=N-OCH_3$, $-CH=CH-N(CH_3)-CH_3$, and $-CH_2-CH=CH-CH_2-SH$.

The term "alkynyl" employed alone or in combination with other terms, means, unless otherwise stated, a stable straight chain or branched hydrocarbon group having the stated number of carbon atoms, and containing one or two carbon-carbon triple bonds, such as ethynyl, 1- and 3-propynyl, 4-but-1-ynyl, and the higher homologs and isomers.

The term "alkoxy" employed alone or in combination with other terms, means, unless otherwise stated, an alkyl group, as defined above, connected to the rest of the molecule via an oxygen atom, such as, for example, methoxy, ethoxy, 1-propoxy, 2-propoxy and the higher homologs and isomers.

The terms "halo" or "halogen" by themselves or as part of another substituent mean, unless otherwise stated, a fluorine, chlorine, bromine, or iodine atom.

The term "aryl" employed alone or in combination with other terms, means, unless otherwise stated, a phenyl, 1-naphthyl, or 2-naphthyl group. The maximal number of substituents allowed on each one of these ring systems is five, seven, and seven, respectively.

Substituents are selected from the group of acceptable substituents listed above.

The term "heteroaryl" by itself or as part of another substituent means, unless otherwise stated, an unsubstituted or substituted, stable, mono- or bicyclic heterocyclic aromatic ring system which consists of carbon atoms and from one to four heteroatoms selected from the group consisting of N, O, and S, and wherein the nitrogen and sulfur heteroatoms may optionally be oxidized, and the nitrogen atom may optionally be quaternized. The heterocyclic system may be attached, unless otherwise stated at any heteroatom or carbon atom which affords a stable structure. The heterocyclic system may be substituted or unsubstituted with one to four substituents independently selected from the list of acceptable aromatic substituents listed above. Examples of such heterocycles include 2-pyrrolyl, 3-pyrrolyl, 3-pyrazolyl, 2-imidazolyl, 4-imidazolyl, pyrazinyl, 2-oxazolyl, 4-oxazolyl, 5-oxazolyl, 3-isoxazolyl, 4-isoxazolyl, 5-isoxazolyl, 2-thiazolyl, 4-thiazolyl, 5-thiazolyl, 2-furyl, 3-furyl, 2-thienyl, 3-thienyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, 2-pyrimidyl, 4-pyrimidyl, 5-benzothiazolyl, purinyl, 2-benzimidazolyl, 5-indolyl, 1-isoquinolyl, 5-isoquinolyl, 2-quinoxalinyl, 5-quinoxalinyl, 3-quinolyl, and 6-quinolyl.

Pharmaceutically acceptable salts of the compounds of Formula I include salts of these compounds with relatively nontoxic acids or bases, depending on the particular substituents found on specific compounds of Formula I. When compounds of Formula I contain relatively acidic functionalities, base addition salts can be obtained by contacting the neutral form of compound I with a sufficient amount of the desired base, either neat or in a suitable inert solvent. Examples of pharmaceutically acceptable base addition salts include sodium, potassium, calcium, ammonium, organic amino, or magnesium salt, or a similar salt. When compounds of Formula I contain relatively basic functionalities, acid addition salts can be obtained by contacting the neutral form of compound I with a sufficient amount of the desired acid, either neat or in a suitable inert solvent. Examples of pharmaceutically acceptable acid addition salts include those derived from inorganic acids like hydrochloric, hydrobromic, nitric, carbonic, monohydrogencarbonic, phosphoric, monohydrogenphosphoric, dihydrogenphosphoric, sulfuric, monohydrogensulfuric, hydriodic, or phosphorous acids and the like, as well as the salts derived from relatively nontoxic organic acids like acetic, propionic, isobutyric, oxalic, maleic, malonic, benzoic, succinic, suberic, fumaric, mandelic, phthalic, benzenesulfonic, p-tolylsulfonic, citric, tartaric, methanesulfonic, and the like. Also included are salts of amino acids such as

arginate and the like, and salts of organic acids like gluconic or galactunoric acids and the like (see, for example, Berge, S.M., et al, "Pharmaceutical Salts", *Journal of Pharmaceutical Science*, Vol. 66, pages 1-19 (1977)). Certain specific compounds of Formula I contain both basic and acidic functionalities that allow the compounds to be converted into either base or acid addition salts.

The free base form may be regenerated by contacting the salt with a base or acid and isolating the parent compound in the conventional manner. The parent form of the compound differs from the various salt forms in certain physical properties, such as solubility in polar solvents, but otherwise the salts are equivalent to the parent form of the compound for the purposes of the present invention.

Certain compounds of the present invention can exist in unsolvated forms as well as solvated forms, including hydrated forms. In general, the solvated forms are equivalent to unsolvated forms and are intended to be encompassed within the scope of the present invention.

Certain compounds of the present invention possess asymmetric carbon atoms (optical centers); the racemates, diastereomers, and individual isomers are all intended to be encompassed within the scope of the present invention.

The compounds of the present invention may also contain unnatural proportions of atomic isotopes at one or more of the atoms that constitute such compounds. For example, the compounds may be radiolabeled with radioactive isotopes, such as for example tritium (^3H) or carbon-14 (^{14}C). All isotopic variations of the compounds of the present invention, whether radioactive or not, are intended to be encompassed within the scope of the present invention.

In various preferred embodiments of the pharmaceutical compositions of compounds of formula I, Y is $S(O_2)$ and Z is NR^1R^2, wherein R^1 is hydrogen or methyl, and R^2 is a substituted phenyl, preferably mono-, di-, or trisubstituted as follows. In one group of preferred compounds, Y is $S(O_2)$ and Z is NR^1R^2, wherein R^1 is hydrogen or methyl, and R^2 is a phenyl group, preferably substituted in the para position by one of the following groups: hydroxy, amino, (C1-C10)alkoxy, (C1-C10)alkyl, (C1-C10)alkylamino, and [di(C1-C10)alkyl]amino, with up to four additional substituents independently chosen from hydrogen, halogen, (C1-C10)alkoxy, (C1-C10)alkyl, and [di(C1-C10)alkyl]amino. Also preferred are compounds of formula I where there is no linking group E between R^1 and R^2.

Illustrative examples of pharmaceutical compositions and compounds of the subject pharmaceutical methods include:

2-Fluoro-1-methoxy-4-pentafluorophenylsulfinamidobenzene;

4-Dimethylamino-1-pentafluorophenylsulfinamidobenzene;

4-Methyl-6-methoxy-2-pentafluorophenylsulfonamidopyrimidine;

4,6-Dimethoxy-2-pentafluorophenylsulfonamidopyrimidine;

2-Pentafluorophenylsulfonamidothiophene;

3-Pentafluorophenylsulfonamidothiophene;

3-Pentafluorophenylsulfonamidopyridine;

4-Pentafluorophenylsulfonamidopyridine;

4-(*N,N,*-Dimethylamino)-1-(*N*-ethylpentafluorophenylsulfonamido)-benzene;

4-*tert*-Butoxy-1-pentafluorophenylsulfonamidobenzene;

3-*tert*-Butoxy-1-pentafluorophenylsulfonamidobenzene;

2-*tert*-Butoxy-1-pentafluorophenylsulfonamidobenzene;

4-Isopropoxy-1-pentafluorophenylsulfonamidobenzene;

3-Isopropoxy-1-pentafluorophenylsulfonamidobenzene;

2-Isopropoxy-1-pentafluorophenylsulfonamidobenzene;

2-Methoxy-1,3-difluoro-5-pentafluorophenylsulfonamidobenzene;

4-Cyclopropoxy-1-pentafluorophenylsulfonamidobenzene;

3-Fluoro-4-cyclopropoxy-1-pentafluorophenylsulfonamidobenzene;

3-Hydroxy-4-cyclopropoxy-1-pentafluorophenylsulfonamidobenzene;

1-Hydroxy-2,3-methylenedioxy-5-pentafluorophenylsulfonamidobenzene;

1-Hydroxy-2,3-ethylenedioxy-5-pentafluorophenylsulfonamidobenzene;

1-Hydroxy-2,3-carbodioxy-5-pentafluorophenylsulfonamidobenzene;

1,3-Dihydroxy-2-ethoxy-5-pentafluorophenylsulfonamidobenzene;

1-Pentafluorophenylsulfonylindole;

1-Pentafluorophenylsulfonyl(2,3-dihydro)indole;

1-Pentafluorophenylsulfonyl(1,2-dihydro)quinoline;

1-Pentafluorophenylsulfonyl(1,2,3,4-tetrahydro)quinoline;

3,4-Difluoro-1-pentafluorophenylsulfonamidobenzene;

4-Trifluoromethoxy-1-pentafluorophenylsulfonamidobenzene;

2-Chloro-5-pentafluorophenylsulfonamidopyridine;

2-Hydroxy-1-methoxy-4-[N-5-hydroxypent-1-yl)pentafluorophenyl-sulfonamido]benzene;

4-(1,1-Dimethyl)ethoxy-1-pentafluorophenylsulfonamidobenzene;

1-Bromo-3-hydroxy-4-methoxy-1-pentafluorophenylsulfonamidobenzene;

2-Bromo-4-methoxy-5-hydroxy-1-pentafluorophenylsulfonamidobenzene;

1-Bromo-4-fluoro-5-methoxy-2-pentafluorophenylsulfonamidobenzene;

3-Chloro-1-pentafluorophenylsulfonamidobenzene;

4-Chloro-1-pentafluorophenylsulfonamidobenzene;

3-Nitro-1-pentafluorophenylsulfonamidobenzene;

4-Methoxy-1-pentafluorophenylsulfonamido-3-(trifluoromethyl)benzene;

4-Methoxy-1-[N-(2-propenyl)pentafluorophenylsulfonamido]benzene;

1-(N-(3-Butenyl)pentafluorophenylsulfonamido)-4-methoxybenzene;

4-Methoxy-1-(N-(4-pentenyl)pentafluorophenylsulfonamido)benzene;

1-[N-(2,3-Dihydroxypropyl)pentafluorophenylsulfonamido]-4-methoxy-benzene;

1-(N-(3,4-Dihydroxybutyl)pentafluorophenylsulfonamido)-4-methoxybenzene;

1-(N-(4,5-Dihydroxypentyl)pentafluorophenylsulfonamido)-4-methoxybenzene;

1-(N-(4-hydroxybutyl)pentafluorophenylsulfonamido)-4-methoxybenzene;

4-Methoxy-1-(N-(5-hydroxypentyl)pentafluorophenylsulfonamido)-benzene;

3-Amino-4-methoxy-1-pentafluorophenylsulfonamidobenzene;

4-Butoxy-1-pentafluorophenylsulfonamidobenzene;

1-Pentafluorophenylsulfonamido-4-phenoxybenzene;

6-Pentafluorophenylsulfonamidoquinoline;

2,3-Dihydro-5-pentafluorophenylsulfonamidoindole;

5-Pentafluorophenylsulfonamidobenzo[a]thiophene;

5-Pentafluorophenylsulfonamidobenzo[a]furan;

3-Hydroxy-4-(1-propenyl)-1-pentafluorophenylsulfonamidobenzene;

4-Benzyloxy-1-pentafluorophenylsulfonamidobenzene;

4-Methylmercapto-1-pentafluorophenylsulfonamidobenzene;

2-Methoxy-1-pentafluorophenylsulfonamidobenzene;

4-Allyloxy-1-pentafluorophenylsulfonamidobenzene;

1-Pentafluorophenylsulfonamido-4-propoxybenzene;

4-(1-Methyl)ethoxy-1-pentafluorophenylsulfonamidobenzene;

1,2-Methylenedioxy-4-pentafluorophenylsulfonamidobenzene;

1,2-Dimethoxy-4-pentafluorophenylsulfonamidobenzene;

4-(*N,N*-Diethylamino)-1-pentafluorophenylsulfonamidobenzene;

4-Amino-1-pentafluorophenylsulfonamidobenzene;

Pentafluorophenylsulfonamidobenzene;

5-Pentafluorophenylsulfonamidoindazole;

4-(*N,N*-Dimethylamino)-1-(*N*-methylpentafluorophenylsulfonamido)-benzene;

1,2-Dihydroxy-4-pentafluorophenylsulfonamidobenzene;

3,5-Dimethoxy-1-pentafluorophenylsulfonamidobenzene;

3-Ethoxy-1-pentafluorophenylsulfonamidobenzene;

7-Hydroxy-2-pentafluorophenylsulfonamidonaphthalene;

3-Phenoxy-1-pentafluorophenylsulfonamidobenzene;

4-(1-Morpholino)-1-pentafluorophenylsulfonamidobenzene;

5-Pentafluorophenylsulfonamido-1,2,3-trimethoxybenzene;

2-Hydroxy-1,3-methoxy-5-pentafluorophenylsulfonamidobenzene;

1,2-Dihydroxy-3-methoxy-5-pentafluorophenylsulfonamidobenzene;

5-Pentafluorophenylsulfonamido-1,2,3-trihydroxybenzene;

3-Hydroxy-5-methoxy-1-pentafluorophenylsulfonamidobenzene;

3,5-Dihydroxy-1-pentafluorophenylsulfonamidobenzene;

2-Fluoro-1-methoxy-4-(*N*-methylpentafluorophenylsulfonamido)benzene;

4-(*N,N*-Dimethylamino)-1-pentafluorophenylsulfonamidobenzene, hydrochloride;

2-Methoxy-5-pentafluorophenylsulfonamidopyridine; and

2-Anilino-3-pentafluorophenylsulfonamidopyridine.

Examples of the most preferred pharmaceutical compositions and compounds of the subject pharmaceutical methods include:

4-(*N,N*-Dimethylamino)-1-pentafluorophenylsulfonamidobenzene;

3-(*N,N*-Dimethylamino)-1-pentafluorophenylsulfonamidobenzene;

1,2-Ethylenedioxy-4-pentafluorophenylsulfonamidobenzene;

2-Hydroxy-1-methoxy-4-pentafluorophenylsulfonamidobenzene;

2-Fluoro-1-methoxy-4-pentafluorophenylsulfonamidobenzene;

2-Hydroxy-1-methoxy-4-pentafluorophenylsulfonamidobenzene, sodium salt;

2-Hydroxy-1-methoxy-4-pentafluorophenylsulfonamidobenzene, potassium salt;

2-Fluoro-1-methoxy-4-pentafluorophenylsulfonamidobenzene, sodium salt;

2-Fluoro-1-methoxy-4-pentafluorophenylsulfonamidobenzene, potassium salt;

4-Methoxy-1-pentafluorophenylsulfonamidobenzene;

3-Hydroxy-1-pentafluorophenylsulfonamidobenzene;

4-Hydroxy-1-pentafluorophenylsulfonamidobenzene;

1,2-Dimethyl-4-pentafluorophenylsulfonamidobenzene;

5-Pentafluorophenylsulfonamidoindole;

4-Ethoxy-1-pentafluorophenylsulfonamidobenzene;

3-Methoxy-1-pentafluorophenylsulfonamidobenzene;

2-Bromo-1-methoxy-4-pentafluorophenylsulfonamidobenzene;

2-Chloro-1-methoxy-4-pentafluorophenylsulfonamidobenzene;

2-Bromo-3-hydroxy-4-methoxy-1-pentafluorophenylsulfonamidobenzene;

2-Bromo-4-methoxy-5-hydroxy-1-pentafluorophenylsulfonamidobenzene;

1-Bromo-4-fluoro-5-methoxy-2-pentafluorophenylsulfonamidobenzene;

4-Chloro-1-pentafluorophenylsulfonamidobenzene; and

3-Amino-4-methoxy-1-pentafluorophenylsulfonamidobenzene.

The invention provides for certain novel compounds of general Formula I that possess one or more valuable biological activities such as a pharmacologic, toxicologic, metabolic, etc. Exemplary compounds of this embodiment of the invention include:

2-Fluoro-1-methoxy-4-pentafluorophenylsulfinamidobenzene;

4-Dimethylamino-1-pentafluorophenylsulfinamidobenzene;

4-Methyl-6-methoxy-2-pentafluorophenylsulfonamidopyrimidine;

4,6-Dimethoxy-2-pentafluorophenylsulfonamidopyrimidine;

2-Pentafluorophenylsulfonamidothiophene;

3-Pentafluorophenylsulfonamidothiophene;

3-Pentafluorophenylsulfonamidopyridine;

4-Pentafluorophenylsulfonamidopyridine;

4-(*N,N,*-Dimethylamino)-1-(*N*-ethylpentafluorophenylsulfonamido) benzene;

4-*tert*-Butoxy-1-pentafluorophenylsulfonamidobenzene;

3-*tert*-Butoxy-1-pentafluorophenylsulfonamidobenzene;

2-*tert*-Butoxy-1-pentafluorophenylsulfonamidobenzene;

4-Isopropoxy-1-pentafluorophenylsulfonamidobenzene;

3-Isopropoxy-1-pentafluorophenylsulfonamidobenzene;

2-Isopropoxy-1-pentafluorophenylsulfonamidobenzene;

2-Methoxy-1,3-difluoro-5-pentafluorophenylsulfonamidobenzene;

1-Hydroxy-2,3-methylenedioxy-5-pentafluorophenylsulfonamidobenzene;

1-Hydroxy-2,3-ethylenedioxy-5-pentafluorophenylsulfonamidobenzene;

1-Hydroxy-2,3-carbodioxy-5-pentafluorophenylsulfonamidobenzene;

1,3-Dihydroxy-2-ethoxy-5-pentafluorophenylsulfonamidobenzene;

1-Pentafluorophenylsulfonylindole;

1-Pentafluorophenylsulfonyl(2,3-dihydro)indole;

1-Pentafluorophenylsulfonyl(1,2-dihydro)quinoline;

1-Pentafluorophenylsulfonyl(1,2,3,4-tetrahydro)quinoline;

3,4-Difluoro-1-pentafluorophenylsulfonamidobenzene;

4-Trifluoromethoxy-1-pentafluorophenylsulfonamidobenzene;

2-Chloro-5-pentafluorophenylsulfonamidopyridine;

2-Hydroxy-1-methoxy-4-[N-5-hydroxypent-1-yl)pentafluorophenyl-sulfonamido]benzene;

4-(1,1-Dimethyl)ethoxy-1-pentafluorophenylsulfonamidobenzene;

1-Bromo-3-hydroxy-4-methoxy-1-pentafluorophenylsulfonamidobenzene;

2-Bromo-4-methoxy-5-hydroxy-1-pentafluorophenylsulfonamidobenzene;

1-Bromo-4-fluoro-5-methoxy-2-pentafluorophenylsulfonamidobenzene;

3-Chloro-1-pentafluorophenylsulfonamidobenzene;

4-Chloro-1-pentafluorophenylsulfonamidobenzene;

3-Nitro-1-pentafluorophenylsulfonamidobenzene;

4-Methoxy-1-pentafluorophenylsulfonamido-3-(trifluoromethyl)benzene;

4-Methoxy-1-[N-(2-propenyl)pentafluorophenylsulfonamido]benzene;

1-(N-(3-Butenyl)pentafluorophenylsulfonamido)-4-methoxybenzene;

4-Methoxy-1-(N-(4-pentenyl)pentafluorophenylsulfonamido)benzene;

1-[N-(2,3-Dihydroxypropyl)pentafluorophenylsulfonamido]-4-methoxy-benzene;

1-(N-(3,4-Dihydroxybutyl)pentafluorophenylsulfonamido)-4-methoxybenzene;

1-(N-(4,5-Dihydroxypentyl)pentafluorophenylsulfonamido)-4-methoxybenzene;

1-(N-(4-hydroxybutyl)pentafluorophenylsulfonamido)-4-methoxybenzene;

4-Methoxy-1-(N-(5-hydroxypentyl)pentafluorophenylsulfonamido)-benzene;

3-Amino-4-methoxy-1-pentafluorophenylsulfonamidobenzene;

4-Butoxy-1-pentafluorophenylsulfonamidobenzene;

1-Pentafluorophenylsulfonamido-4-phenoxybenzene;

4-Benzyloxy-1-pentafluorophenylsulfonamidobenzene;

4-Methylmercapto-1-pentafluorophenylsulfonamidobenzene;

2-Methoxy-1-pentafluorophenylsulfonamidobenzene;

4-Allyloxy-1-pentafluorophenylsulfonamidobenzene;

1-Pentafluorophenylsulfonamido-4-propoxybenzene;

4-(1-Methyl)ethoxy-1-pentafluorophenylsulfonamidobenzene;

1,2-Methylenedioxy-4-pentafluorophenylsulfonamidobenzene;

1,2-Dimethoxy-4-pentafluorophenylsulfonamidobenzene;

4-(*N,N*-Diethylamino)-1-pentafluorophenylsulfonamidobenzene;

4-Amino-1-pentafluorophenylsulfonamidobenzene;

Pentafluorophenylsulfonamidobenzene;

5-Pentafluorophenylsulfonamidoindazole;

4-(*N,N*-Dimethylamino)-1-(*N*-methylpentafluorophenylsulfonamido)-benzene;

1,2-Dihydroxy-4-pentafluorophenylsulfonamidobenzene;

3,5-Dimethoxy-1-pentafluorophenylsulfonamidobenzene;

3-Ethoxy-1-pentafluorophenylsulfonamidobenzene;

7-Hydroxy-2-pentafluorophenylsulfonamidonaphthalene;

3-Phenoxy-1-pentafluorophenylsulfonamidobenzene;

4-(1-Morpholino)-1-pentafluorophenylsulfonamidobenzene;

5-Pentafluorophenylsulfonamido-1,2,3-trimethoxybenzene;

2-Hydroxy-1,3-methoxy-5-pentafluorophenylsulfonamidobenzene;

1,2-Dihydroxy-3-methoxy-5-pentafluorophenylsulfonamidobenzene;

5-Pentafluorophenylsulfonamido-1,2,3-trihydroxybenzene;

4-Cyclopropoxy-1-pentafluorophenylsulfonamidobenzene;

3-Fluoro-4-cyclopropoxy-1-pentafluorophenylsulfonamidobenzene;

6-Pentafluorophenylsulfonamidoquinoline;

2,3-Dihydro-5-pentafluorophenylsulfonamidoindole;

5-Pentafluorophenylsulfonamidobenzo[a]thiophene;

5-Pentafluorophenylsulfonamidobenzo[a]furan;

3-Hydroxy-4-(1-propenyl)-1-pentafluorophenylsulfonamidobenzene;

3-Hydroxy-5-methoxy-1-pentafluorophenylsulfonamidobenzene;

3,5-Dihydroxy-1-pentafluorophenylsulfonamidobenzene;

2-Fluoro-1-methoxy-4-(*N*-methylpentafluorophenylsulfonamido)benzene;

4-(*N,N*-Dimethylamino)-1-pentafluorophenylsulfonamidobenzene, hydrochloride; and,

2-Analino-3-pentafluorophenylsulfonamidopyridine.

Preferred compounds of this embodiment of the invention have specific pharmacological properties. Examples of the most preferred compounds of this embodiment of the invention include:

4-(*N,N*-Dimethylamino)-1-pentafluorophenylsulfonamidobenzene:

3-(*N,N*-Dimethylamino)-1-pentafluorophenylsulfonamidobenzene;

1,2-Ethylenedioxy-4-pentafluorophenylsulfonamidobenzene;

2-Hydroxy-1-methoxy-4-pentafluorophenylsulfonamidobenzene;

2-Fluoro-1-methoxy-4-pentafluorophenylsulfonamidobenzene;

2-Hydroxy-1-methoxy-4-pentafluorophenylsulfonamidobenzene, sodium salt;

2-Hydroxy-1-methoxy-4-pentafluorophenylsulfonamidobenzene, potassium salt;

2-Fluoro-1-methoxy-4-pentafluorophenylsulfonamidobenzene, sodium salt;

2-Fluoro-1-methoxy-4-pentafluorophenylsulfonamidobenzene, potassium salt;

4-Methoxy-1-pentafluorophenylsulfonamidobenzene;

3-Hydroxy-1-pentafluorophenylsulfonamidobenzene;

4-Hydroxy-1-pentafluorophenylsulfonamidobenzene;

1,2-Dimethyl-4-pentafluorophenylsulfonamidobenzene;

5-Pentafluorophenylsulfonamidoindole;

4-Ethoxy-1-pentafluorophenylsulfonamidobenzene;

3-Methoxy-1-pentafluorophenylsulfonamidobenzene;

2-Bromo-1-methoxy-4-pentafluorophenylsulfonamidobenzene;

2-Chloro-1-methoxy-4-pentafluorophenylsulfonamidobenzene;

2-Bromo-3-hydroxy-4-methoxy-1-pentafluorophenylsulfonamidobenzene;

2-Bromo-4-methoxy-5-hydroxy-1-pentafluorophenylsulfonamidobenzene;

1-Bromo-4-fluoro-5-methoxy-2-pentafluorophenylsulfonamidobenzene;

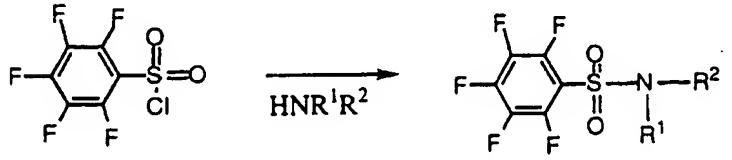
4-Chloro-1-pentafluorophenylsulfonamidobenzene; and

3-Amino-4-methoxy-1-pentafluorophenylsulfonamidobenzene.

SYNTHESIS

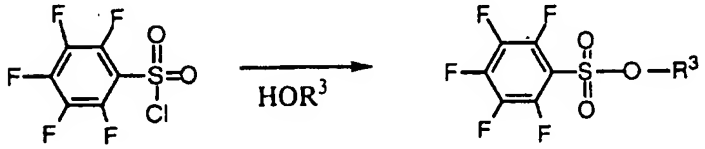
Scheme I

Syntheses of pentafluorophenylsulfonamides, sulfonic esters, sulfinamides, and sulfinic esters



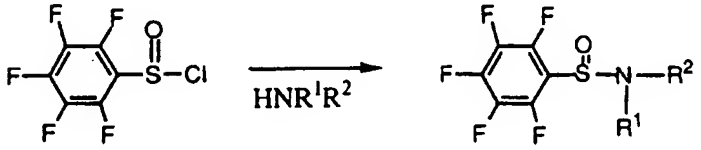
1

Sulfonamide



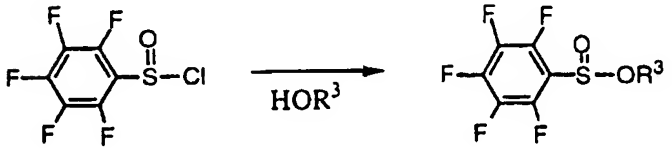
2

Sulfonic ester



3

Sulfinamide

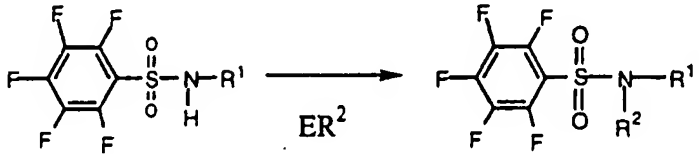


4

Sulfinic ester

Scheme II

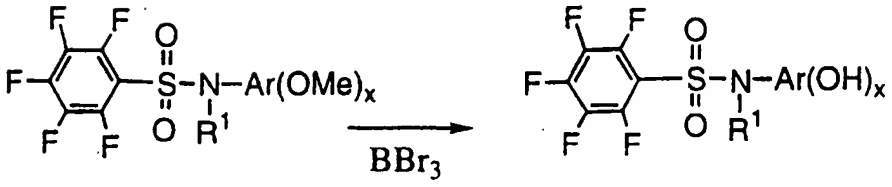
Alternative synthesis of *N,N*-disubstituted pentafluorophenylsulfonamides.



1

Scheme III

Syntheses of phenols



5

x=1-3

The invention provides methods of making the subject compounds and compositions. In one general embodiment, the methods involve combining pentafluorophenylsulfonyl chloride with an amine having the general formula R^1R^2NH under conditions whereby the pentafluorophenylsulfonyl chloride and amine react to form the desired compound, and isolating the compound.

Compounds with the generic structure 1 or 3 (Scheme I) may be prepared by reacting the appropriate starting amine in a solvent such as tetrahydrofuran (THF), dimethylformamide (DMF), ether, toluene or benzene in the presence of a base such as pyridine, *p*-dimethylaminopyridine, triethylamine, sodium carbonate or potassium carbonate and pentafluorophenylsulfonyl chloride or pentafluorophenylsulfinyl chloride, respectively. Pyridine itself may also be used as the solvent. Preferred solvents are pyridine and DMF and preferred bases are pyridine, triethylamine, and potassium carbonate. This reaction can be carried out at a temperature range of 0 ^{0}C to 100 ^{0}C, conveniently at ambient temperature.

Compounds of the generic structure 1 can also be obtained by treating the starting sulfonamide (Scheme II) with a base such as LDA, NaH, dimsyl salt, alkyl lithium, potassium carbonate, under an inert atmosphere such as argon or nitrogen, in a solvent such as benzene, toluene, DMF or THF with an alkylating group containing a leaving group such a Cl, Br, I, MsO-, TsO-, TFAO-, represented by E in Scheme II. A preferred solvent for this reaction is THF and the preferred base is lithium bis(trimethylsilyl)amide. This reaction can be carried out at a temperature range of 0 ^{0}C to 100 ^{0}C, conveniently at ambient temperature.

Sulfonic esters (2) and sulfinic esters (4) may be prepared by reacting the appropriate starting phenol in a solvent such as THF, DMF, toluene or benzene in the presence of a base such as pyridine, triethylamine, sodium carbonate, potassium carbonate or 4-dimethylaminopyridine with pentafluorophenylsulfonyl chloride or pentafluorophenylsulfinyl chloride, respectively. Pyridine itself may also be used as the solvent. Preferred solvents are pyridine and DMF and preferred bases are sodium carbonate and potassium carbonate. This reaction can be carried out at a temperature range of 0 ^{0}C to 100 ^{0}C, conveniently at ambient temperature.

Compounds of the general structure 5, in which Ar is an aromatic group and x is from one to three, can be obtained from the corresponding methyl ethers (Scheme III) by reaction

with boron tribromide in a solvent of low polarity such as hexanes or CH_2Cl_2 under an inert atmosphere at a temperature ranging from -45° to 30 °C. In a preferred embodiment, the reaction is carried out in CH_2Cl_2 at about 30 °C.

Occasionally, the substrates for the transformations shown in Schemes I-III may contain functional groups (for example, amino, hydroxy or carboxy) which are not immediately compatible with the conditions of the given reaction. In such cases, these groups may be protected with a suitable protective group, and this protective group removed subsequent to the transformation to give the original functionality using well know procedures such as those illustrated in T.W. Greene and P.G. M. Wuts, Protective Groups in Organic Synthesis, Second Edition, John Wiley & Sons. Inc., 1991.

The compounds used as initial starting materials in this invention may be purchased from commercial sources or alternatively are readily synthesized by standard procedures which are well know to those of ordinary skill in the art.

Some of the compounds of formula I may exist as stereoisomers, and the invention includes all active stereoisomeric forms of these compounds. In the case of optically active isomers, such compounds may be obtained from corresponding optically active precursors using the procedures described above or by resolving racemic mixtures. The resolution may be carried out using various techniques such as chromatography, repeated recrystallization of derived asymmetric salts, or derivatization, which techniques are well known to those of ordinary skill in the art.

The compounds of formula I which are acidic or basic in nature can form a wide variety of salts with various inorganic and organic bases or acids, respectively. These salts must be pharmacologically acceptable for administration to mammals. Salts of the acidic compounds of this invention are readily prepared by treating the acid compound with an appropriate molar quantity of the chosen inorganic or organic base in an aqueous or suitable organic solvent and then evaporating the solvent to obtain the salt. Acid addition salts of the basic compounds of this invention can be obtained similarly by treatment with the desired inorganic or organic acid and subsequent solvent evaporation and isolation.

The compounds of the invention may be labeled in a variety of ways. For example, the compounds may be provided as radioactive isotopes; for example, tritium and the ^{14}C-isotopes. Similarly, the compounds may be advantageously joined, covalently or

noncovalently, to a wide variety of joined compounds which may provide pro-drugs or function as carriers, labels, adjuvents, coactivators, stabilizers, etc. Hence, compounds having the requisite structural limitations encompass such compounds joined directly or indirectly (e.g. through a linker molecule), to such joined compounds.

A wide variety of indications may be treated, either prophylactically or therapeutically, with the compounds and compositions of the present invention. For example, the subject compounds and compositions have been found to be effective modulators of cell proliferation. Limitation of cell growth is effected by contacting a target cell, *in* or *ex vivo*, with an effective amount of one or more of the subject compositions or compounds. Compounds may be assayed for their ability to modulate cellular proliferation using cell and animal models to evaluate cell growth inhibition and cytotoxicity, which models are known in the art, but are exemplified by the method of S.A. Ahmed et al. (1994) J. Immunol. Methods 170: 211-224, for determining the effects of compounds on cell growth.

Conditions amenable to treatment by the compounds and compositions of the present invention include any state of undesirable cell growth, including various neoplastic diseases, abnormal cellular proliferations and metastatic diseases, where any of a wide variety of cell types may be involved, including cancers such as Kaposi's sarcoma, Wilms tumor, lymphoma, leukemia, myeloma, melanoma, breast, ovarian, lung, etc. and others such as cystic disease, cataracts, psoriasis, etc. Other conditions include restenosis, where vascular smooth muscle cells are involved, inflammatory disease states, where endothelial cells, inflammatory cells and glomerular cells are involved, myocardial infarction, where heart muscle cells are involved, glomerular nephritis, where kidney cells are involved, transplant rejection, where endothelial cells are involved, infectious diseases such as HIV infection and malaria, where certain immune cells and/or other infected cells are involved, and the like. Infectious and parasitic agents per se (e.g. trypanosomes, fungi, etc) are also subject to selective proliferative control using the subject compositions and compounds.

Many of the subject compounds have been shown to bind to the ß-subunit of tubulin and interfere with normal tubulin function. Hence, the compounds provide agents for modulating cytoskeletal structure and/or function. Preferred compounds bind irreversibly or covalently, and hence provide enhanced application over prior art microtubule disruptors such as colchicine. The compositions may be advantageously combined and/or used in

combination with other antiproliferative chemotherapeutic agents. different from the subject compounds (see Margolis et al. (1993) US Pat No. 5,262,409). Additional relevant literature includes: Woo et al. (1994) WO94/08041; Bouchard et al. (1996) WO96/13494; Bombardelli et al. (1996) WO96/11184; Bonura et al. (1992) WO92/15291.

ANALYSIS

The subject compositions were demonstrated to have pharmacological activity in *in vitro* and *in vivo* assays, e.g. are capable of specifically modulating a cellular physiology to reduce an associated pathology or provide or enhance a prophylaxis. Preferred compounds display specific toxicity to various types of cells. Certain compounds and compositions of the present invention exert their cytotoxic effects by interacting with cellular tubulin. For certain preferred compounds and compositions of the present invention, that interaction is covalent and irreversible. For example, exposure of a wide variety of tissue and cell samples, e.g. human breast carcinoma MCF7 cells, to tritiated forms of these preferred compounds, e.g. Compound 7 (Example 72), results in the irreversible labeling of only one detectable cellular protein, which was found to be tubulin. This protein is a key component of microtubules, which constitute the cytoskeleton and also play critical roles in many other aspects of the cell's physiology, including cell division. The labeling of tubulin by the subject preferred compounds is also shown to be dose-dependent. The site of covalent binding on tubulin is identified as Cysteine-239 on the ß-tubulin chain. The same Cys-239 residue is selectively covalently modified when present in a wide variety of Cys-239 containing ß-tubulin petides (e.g. Ser-234 to Met-267) provided in vitro or in vivo. Consistent with the ability of these compounds to bind to ß-tubulin, treatment of a wide variety of cell and tissue types with various concentrations of the compounds resulted in widespread, irreversible disruption of the cytoskeleton of most cells.

As discribed *inter alia* in Luduena (1993) Mol Biol of the Cell 4, 445-457, tubulin defines a family of heterodimers of two polypeptides, designated α and ß. Moreover, animals express multiple forms (isotypes) of each α and ß polypeptides from multiple a and ß genes. Many ß isotypes comprise a conserved cysteine, Cys-239 (of human ß2 tubulin: because of upstream sequence variations, the absolute position of Cys-239 is subject to variation, though Cys-239 is readily identified by those in the art by its relative position (i.e.

context within encompassing consensus sequence, e.g. at least 8, preferably 12. more preferably 16, most preferably 20 residue consensus peptide region of the isotype or fragment thereof, which region contains Cys-239). By selective binding to Cys-239 is meant that Cys-239 is preferentially bound relative to all other residues, including cysteins of the protein, by at least at least a factor of 2, preferably 10, more preferably 100, most preferably 1,000. In a particularly prefered embodiment, Cys-239 is substantially exclusively and preferably exclusive bound. By selective binding to or modification of tubulin is meant that tubulin is preferentially modified relative to all other proteins, by at least a factor of 2, preferably 10, more preferably 100, most preferably 1,000. In a particularly prefered embodiment, tubulin is substantially exclusively and preferably exclusive modified.

Compounds may be evaluated *in vitro* for their ability to inhibit cell growth, for example, as described in S.A. Ahmed et al. (1994) J. Immunol. Methods 170:211-224. In addition, established animal models to evaluate antiproliferative effects of compounds are known in the art. For example, several of the compounds disclosed herein are shown to inhibit the growth of human tumors, including MDR and taxol and/or vinblastine-restistant tumors, grafted into immunodeficient mice (using methodology similar to that reported by J. Rygaard and C.O. Povlsen (1969) Acta Pathol. Microbiol. Scand. 77:758-760, and reviewed by B.C. Giovanella and J. Fogh (1985) Adv. Cancer Res. 44:69-120.

FORMULATION AND ADMINISTRATION

The invention provides methods of using the subject compounds and compositions to treat disease or provide medicinal prophylaxis, to slow down and/or reduce the growth of tumors, to treat bacterial infections, etc. These methods generally involve contacting cells with or administering to the host an effective amount of the subject compounds or pharmaceutically acceptable compositions.

The compositions and compounds of the invention and the pharmaceutically acceptable salts thereof can be administered in any effective way such as via oral, parenteral or topical routes. Generally, the compounds are administered in dosages ranging from about 2 mg up to about 2,000 mg per day, although variations will necessarily occur depending on the disease target, the patient, and the route of administration. Preferred dosages are administered orally in the range of about 0.05 mg/kg to about 20 mg/kg, more preferably in the range of

about 0.05 mg/kg to about 2 mg/kg, most preferably in the range of about 0.05 mg/kg to about 0.2 mg per kg of body weight per day.

In one embodiment, the invention provides the subject compounds combined with a pharmaceutically acceptable excipient such as sterile saline or other medium, water, gelatin, an oil, etc. to form pharmaceutically acceptable compositions. The compositions and/or compounds may be administered alone or in combination with any convenient carrier, diluent, etc. and such administration may be provided in single or multiple dosages. Useful carriers include solid, semi-solid or liquid media including water and non-toxic organic solvents.

In another embodiment, the invention provides the subject compounds in the form of a pro-drug, which can be metabolically converted to the subject compound by the recipient host. A wide variety of pro-drug formulations are known in the art.

The compositions may be provided in any convenient form including tablets, capsules, lozenges, troches, hard candies, powders, sprays, creams, suppositories, etc. As such the compositions, in pharmaceutically acceptable dosage units or in bulk, may be incorporated into a wide variety of containers. For example, dosage units may be included in a variety of containers including capsules, pills, etc.

The compositions may be advantageously combined and/or used in combination with other antiproliferative therapeutic or prophylactic agents, different from the subject compounds. In many instances, administration in conjunction with the subject compositions enhances the efficacy of such agents. Exemplary antiproliferative agents include cyclophosphamide, methotrexate, adriamycin, cisplatin, daunomycin, vincristine, vinblastine, vinarelbine, paclitaxel, docetaxel, tamoxifen, flutamide, hydroxyurea, and mixtures thereof.

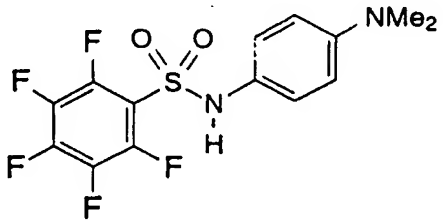
The compounds and compositions also find use in a variety of in vitro and in vivo assays, including diagnostic assays. In certain assays and in in vivo distribution studies, it is desirable to used labeled versions of the subject compounds and compositions, e.g. radioligand displacement assays. Accordingly, the invention provides the subject compounds and compositions comprising a detectable label, which may be spectroscopic (e.g. fluorescent), radioactive, etc.

The following examples are offered by way of illustration and not by way of limitation.

EXAMPLES

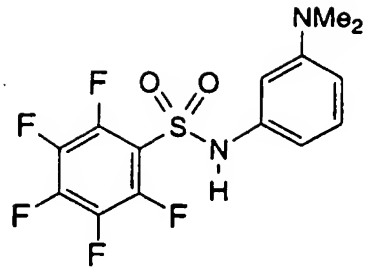
^{1}H NMR spectra were recorded on a Varian Gemini 400MHz NMR spectrometer. Significant peaks are tabulated in the order: multiplicity (s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet), coupling constant(s) in Hertz, number of protons. Electron Ionization (EI) mass spectra were recorded on a Hewlett Packard 5989A mass spectrometer. Fast Atom Bombardment (FAB) mass spectroscopy was carried out in a VG analytical ZAB 2-SE high field mass spectrometer. Mass spectroscopy results are reported as the ratio of mass over charge, and the relative abundance of the ion is reported in parentheses.

Example 1



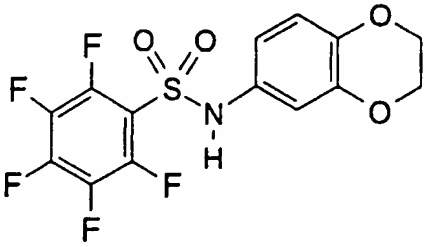
4-(N,N-Dimethylamino)-1-pentafluorophenylsulfonamidobenzene. To *N,N*-dimethyl-1,4-phenyldiamine dihydrochloride (3g, 14.6mmol) suspended in pyridine (50mL) at 0 ^{0}C under argon was added dropwise pentafluorophenylsulfonyl chloride (2.38mL, 16mmol). The reaction mixture was stirred for 30 min at 0 ^{0}C and allowed to warm to ambient temperature. The reaction mixture was stirred at room temperature for 3h. The volume of the mixture was then reduced to 10 mL under reduced pressure. The mixture was diluted with ethyl acetate and the reaction quenched with water. The layers were separated and the aqueous layer extracted twice with ethyl acetate. The organic layers were combined and washed with brine and dried with $MgSO_4$. The solvent was evaporated and the residue purified by chromatography on silica, eluting with CH_2Cl_2. The title product was obtained as a white solid in 63% yield (3.4g). ^{1}H NMR ($CDCl_3$): 7.01(d, *J*=8.9Hz, 2H), 6.77(s, 1H), 6.59(d, *J*=8.3Hz, 2H), 2.92ppm(s, 6H). FAB m/z (relative abundance): 367(100%, M+H$^+$), 135(30%), 121(25%). Anal. calcd. for $C_{14}H_{11}F_5N_2O_2S$: C 45.95, H 3.03, N 7.65. Found C 45.83, H 2.99, N 7.62

Example 2



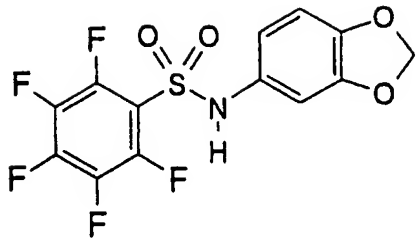
3-(*N,N*-Dimethylamino)-1-pentafluorophenylsulfonamidobenzene. ^{1}H NMR ($CDCl_3$): 7.12(t, *J*=8Hz, 1H), 7.05(s, 1H), 6.57(s, 1H) 6.53(d, *J*=8Hz, 1H), 6.40(d, *J*=8Hz, 1H), 2.94ppm (s, 6H). FAB m/z: 366 (100%, M^+). The compound was prepared by a protocol similar to that of example 1 by replacing *N,N*-dimethyl-1,4-phenyldiamine dihydrochloride with 3-(*N,N*-dimethylamino)aniline.

Example 3



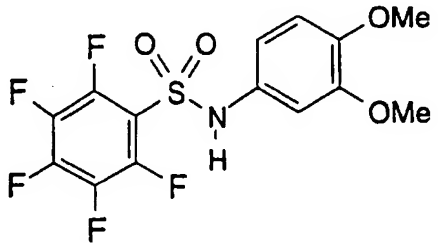
1,2-Ethylenedioxy-4-pentafluorophenylsulfonamidobenzene. ^{1}H NMR ($CDCl_3$): 6.97(s, 1H), 6.76(d, *J*=8.6Hz, 1H), 6.72(d, *J*=2.6Hz, 1H), 6.62(dd, *J*=8.6, 2.6Hz, 1H), 4.21ppm (s, 4H). FAB m/z: 381(100%, $M+H^+$). Anal calcd. for $C_{14}H_8F_5NO_4S$: C 44.09, H 2.12, N 3.68, S 8.39. Found: C 43.83, H 2.19, N 3.62, S 8.20. The compound was prepared by a protocol similar to that of example 1 by replacing *N,N*-dimethyl-1,4-phenyldiamine dihydrochloride with 3,4-ethylenedioxyaniline.

Example 4



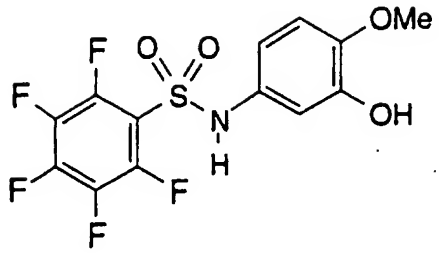
1,2-Methylenedioxy-4-pentafluorophenylsulfonamidobenzene. ^{1}H NMR ($CDCl_3$): 6.85(s, 1H), 6.78 (s, 1H), 6.70(d,*J*=8Hz, 1H), 6.57(d, *J*=8Hz. 1H), 5.97ppm(s, 2H). The compound was prepared by a protocol similar to that of example 1 by replacing *N,N*-dimethyl-1,4-phenyldiamine dihydrochloride with 3,4-methylenedioxyaniline.

Example 5



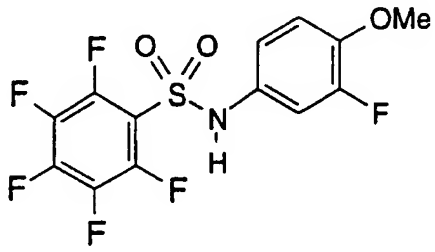
1,2-Dimethoxy-4-pentafluorophenylsulfonamidobenzene. ^{1}H NMR ($CDCl_3$): 6.98(s, 1H), 6.85(d, 1H), 6.74(d, 1H), 6.60(dd, 1H), 3.85(s, 3H). 3.83ppm (s, 3H). EI. m/z: 383(50, M^+), 152(100). The compound was prepared by a protocol similar to that of example 1 by replacing *N,N*-dimethyl-1,4-phenyldiamine dihydrochloride with 3,4-dimethoxyaniline.

Example 6



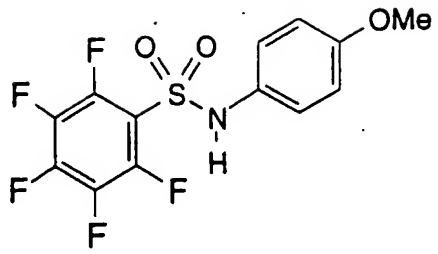
2-Hydroxy-1-methoxy-4-pentafluorophenylsulfonamidobenzene. ^{1}H NMR ($CDCl_3$): 6.93(s, 1H), 6.7-6.8(m, 3H), 5.68(bs, 1H), 3.85ppm(s, 3H). EI, m/z: 333(20, M^+), 138(100). mp 118-120 °C. The compound was prepared by a protocol similar to that of example 1 by replacing *N,N*-dimethyl-1,4-phenyldiamine dihydrochloride with 3-hydroxy-4-methoxyaniline.

Example 7



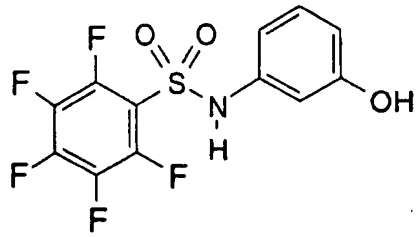
2-Fluoro-1-methoxy-4-pentafluorosulfonamidobenzene.
^{1}H NMR (DMSO) 11.15 (broad s, 1H), 7.13 (t, *J*=9Hz, 1H), 7.02 (dd, *J*=9.5 2.5 Hz, 1H), 6.94ppm (dd, *J*=8.8 1.5Hz, 1H), 3.79ppm (s, 3H). EI, m/z: 371 (20, M^+), 140 (100). Anal. calcd. for $C_{13}H_7HF_6N_1O_3S_1$: C 42.06, H 1.90, N 3.77, S 8.64. Found: C 42.19, H 1.83, N 3.70, S 8.60. Mp 118-119°C. The compound was prepared by a protocol similar to that of example 1 by replacing *N,N*-dimethyl-1,4-phenyldiamine dihydrochloride with 3-fluoro-*p*-anisidine.

Example 8



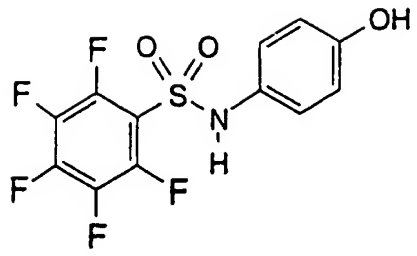
4-Methoxy-1-pentafluorophenylsulfonamidobenzene. ^{1}H NMR ($CDCl_3$): 6.99 (s, 1H), 6.96(d, *J*=4Hz, 2H), 6.88 (d, *J*=4Hz, 2H), 3.83ppm(s, 3H). EI, m/z: 353 (60, M^+), 122 (100). M.p. 102-103 °C. The compound was prepared by a protocol similar to that of example 1 by replacing *N,N*-dimethyl-1,4-phenyldiamine dihydrochloride with 4-methoxyaniline.

Example 9



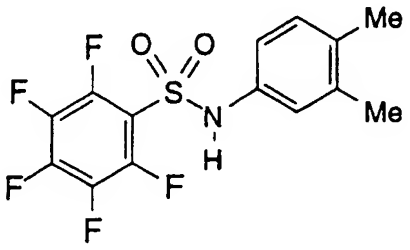
3-Hydroxy-1-pentafluorophenylsulfonamidobenzene. ^{1}H NMR (CD_3OD): 7.15(t, *J*=8.1Hz. 1H), 6.67(t, *J*=2.2Hz, 1H) 6.60(dd, *J*=1.3Hz, 7.8Hz, 1H). 6.52ppm (dd, *J*=2.4Hz 8.3Hz, 1H). EI, m/z: 339 (80, M^-), 256 (50), 81 (100). The compound was prepared by a protocol similar to that of example 1 by replacing *N,N*-dimethyl-1,4-phenyldiamine dihydrochloride with 3-hydroxyaniline.

Example 10



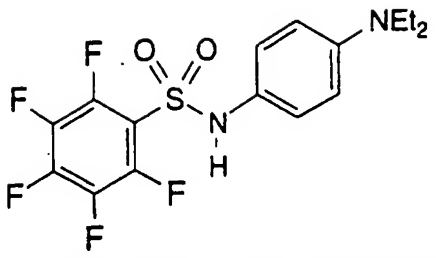
4-Hydroxy-1-pentafluorosulfonamidobenzene. ^{1}H NMR (CD_3OD): 6.95(d, J=8.9Hz, 2H), 6.65ppm (d, J=8.9Hz, 2H). EI, m/z: 339 (30, M^+). The compound was prepared by a protocol similar to that of example 1 by replacing *N,N*-dimethyl-1,4-phenyldiamine dihydrochloride with 4-hydroxyaniline.

Example 11



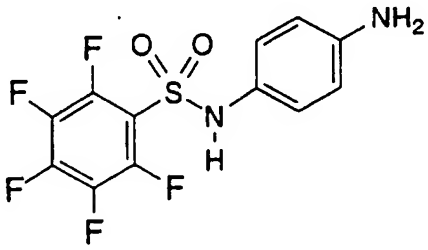
1,2-Dimethyl-4-pentafluorophenylsulfonamidobenzene. ^{1}H NMR ($CDCl_3$): 7.03(d, J=7.9Hz, 1H), 6.92(s, 1H), 6.85-6.82(m, 2H), 2.18(s, 3H), 2.16ppm(s, 3H). The compound was prepared by a protocol similar to that of example 1 by replacing *N,N*-dimethyl-1,4-phenyldiamine dihydrochloride with 3,4-dimethylaniline.

Example 12



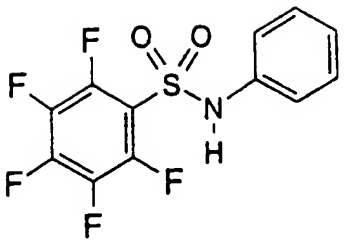
4-(*N,N*-Diethylamino)-1-pentafluorophenylsulfonamidobenzene. ^{1}H NMR ($CDCl_3$): 6.93(d, *J*=8.8Hz, 2H), 6.78(s, 1), 6.45(d, *J*=8.7Hz, 2H), 3.25(dd, *J*=7.0Hz, 7.3Hz,4H), 1.10ppm (t, *J*=7.2Hz, 6H). The compound was prepared by a protocol similar to that of example 1 by replacing *N,N*-dimethyl-1,4-phenyldiamine dihydrochloride with 4-(*N,N*-diethylamino)aniline.

Example 13



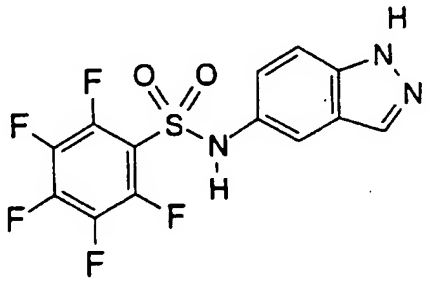
4-Amino-1-pentafluorophenylsulfonamidobenzene. ^{1}H NMR ($CDCl_3$): 6.82(d, *J*=8.7Hz, 2H), 6.49ppm(d, *J*=8.7Hz, 2H). EI, m/z: 338(7, M^+), 107(100), 80(40). The compound was prepared by a protocol similar to that of example 1 by replacing *N,N*-dimethyl-1,4-phenyldiamine dihydrochloride with 1,4-diaminobenzene.

Example 14



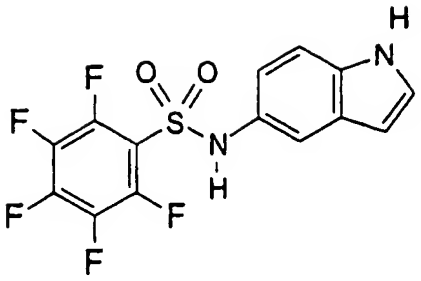
Pentafluorophenylsulfonamidobenzene. ^{1}H NMR ($CDCl_3$): 7.30(d, J=8Hz, 2H), 7.13-7.2(m, 3H), 7.0ppm(s, 1H). EI, m/z: 323(90, M^+), 92(100). The compound was prepared by a protocol similar to that of example 1 by replacing *N,N*-dimethyl-1,4-phenyldiamine dihydrochloride with aniline.

Example 15



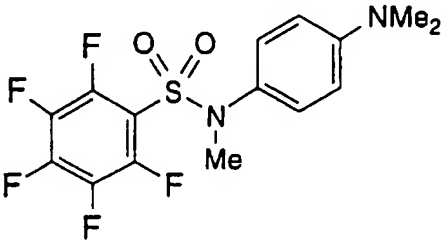
5-Pentafluorophenylsulfonamidoindazole. ^{1}H NMR (CD_3OD): 7.98(s, 1H), 7.69(s, 1H), 7.47(d, J=8.3Hz, 1H), 7.23ppm(d, J=8.3Hz, 1H). EI m/z: 364(50, $M+H^+$), 133(100). The compound was prepared by a protocol similar to that of example 1 by replacing *N,N*-dimethyl-1,4-phenyldiamine dihydrochloride with 5-aminoindazole.

Example 16



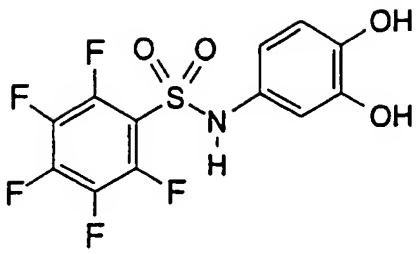
5-Pentafluorophenylsulfonamidoindole. ^{1}H NMR ($CDCl_3$): 8.2(s, 1H), 7.43(s, 1H), 7.3(d, J=8 Hz, 1H), 7.22(s, 1H)), 6.98 (d, J=8 Hz, 1H), 6.92ppm (s, 1H), 6.50ppm(s, 1H). EI m/z: 362(M^+), 131(100). The compound was prepared by a protocol similar to that of example 1 by replacing *N,N*-dimethyl-1,4-phenyldiamine dihydrochloride with 5-aminoindole.

Example 17 .



4-(*N,N*-Dimethylamino)-1-(*N*-methylpentafluorophenylsulfonamido)benzene. 4-(*N,N*-Dimethylamino)-1-(pentafluorophenylsulfonamido)benzene (100mg, 0.273mmol) was dissolved in dry THF (2.5mL) and to the system was added under N_2 at room temperature a 1M solution of lithium *bis*(trimethylsilyl)amide (0.274mL). The reaction mixture was stirred for 10 min followed by addition of MeI (65mg, 0.028mL). The reaction mixture was stirred overnight, the solvent was evaporated under reduced pressure and the crude product purified by HPLC using silica as the stationary phase and eluting with 20%EtOAc/Hex (v/v) to afford the product as a white solid in 60% yield (62mg). EI m/z: 380(35, M^+), 149(100). ^{1}H NMR (CD_3OD) 7.05(d, J=8Hz, 2H), 6.68(d, J=8Hz, 2H), 3.33(s, 3H) 2.93(s, 6H). Anal. calcd. for $C_{15}H_{13}F_5SO_2N_2$: C 47.37, H 3.45, N 7.37. Found: C 47.37, H 3.49, N 7.32.

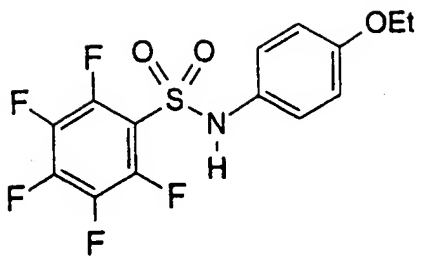
Example 18



1,2-Dihydroxy-4-pentafluorophenylsulfonamidobenzene.

1-Hydroxy-2-methoxy-4-pentafluorophenylsulfonamidobenzene (250mg, 0.678mmol) was suspended in dry CH_2Cl_2 (5mL) at 0 ^{0}C under nitrogen. To the mixture was added BBr_3 as a 1M solution in CH_2Cl_2 (0.746mmol, 1.1eq.). The mixture was warmed to ambient temperature and stirred overnight. The reaction mixture was poured over ice (75mL) and extracted 3 times with 30 mL portions of CH_2Cl_2. The organic layer was dried with $MgSO_4$ and the solvent was evaporated. The crude product was purified by chromatography over silica eluting with 30% (v/v) EtOAc/Hex to afford the product as a white solid in 41% yield (98mg). ^{1}H NMR (DMSO): 10.63(s, 1H), 9.15(s, 1H), 8.91(s, 1H), 6.61(d, *J*=9Hz, 1H), 6.58(d, *J*=3Hz, 1H), 6.39ppm(dd, *J*= 9Hz 3Hz, 1H).

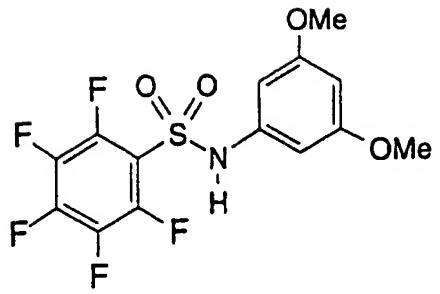
Example 19



4-Ethoxy-1-pentafluorophenylsulfonamidobenzene. To a stirred solution of *p*-phenetidine (0.100g, 0.729mmol) in dimethylformamide (3.65 mL) at 25 ^{0}C was added pentafluorophenyl sulfonyl chloride (0.135mL, 0.911mmol), followed by sodium carbonate (0.116g, 1.09mmol), and the reaction mixture was stirred for 18 hours. The reaction mixture was diluted with ethyl acetate (50mL) and washed with 20% ammonium chloride (2 x 20mL) and saturated sodium chloride (2 x 20mL). The organic layer was dried (sodium sulfite), and the ethyl acetate was removed under reduced pressure to yield a reddish-brown oil. Column chromatography (3:1 ethyl acetate/hexane) yielded the title compound (0.222g, 83%). ^{1}H NMR ($CDCl_3$) 7.08 (d, J = 9Hz, 2H), 7.04 (s, 1H), 6.80 (d. J= 9Hz, 2H), 3.96 (q, J=7Hz, 2H), 1.37 ppm (t, J=7Hz, 2H). IR (neat) 3000-3600, 1750 cm^{-1}. EI m/z : 367(M^+), 154, 136.

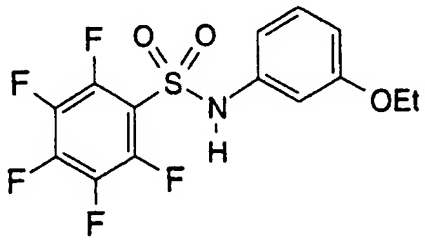
The compounds of Examples 20 through 26 were prepared by a protocol similar to that of Example 19 by replacing *p*-phenetidine with the appropriate amine.

Example 20



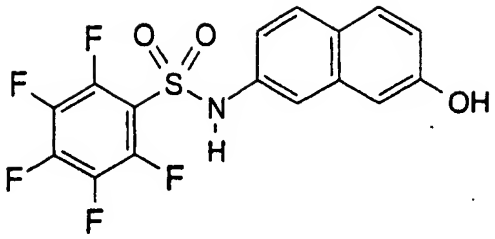
3,5-Dimethoxy-1-pentafluorophenylsulfonamidobenzene . The compound was prepared by a protocol similar to that of Example 19 by replacing *p*-phenetidine with 3,5-dimethoxyaniline. ^{1}H NMR ($CDCl_3$) 6.91(s, 1H), 6.32(s, 2H), 6.25(s, 1H), 3.72ppm(s, 6H).

Example 21



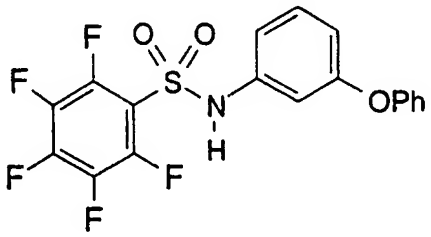
3-Ethoxy-1-pentafluorophenylsulfonamidobenzene . The compound was prepared by a protocol similar to that of Example 19 by replacing *p*-phenetidine with 3-ethoxyaniline. ^{1}H NMR ($CDCl_3$) 7.35 (t, J = 8Hz, 1H), 7.21(s, 1H), 6.92(s, 1H), 6.86(d, J=8Hz, 1H), 6.83(d, J=8Hz, 1H), 4.15(q, J=6Hz, 2H), 1.56ppm (t, J=6Hz, 3H).

Example 22



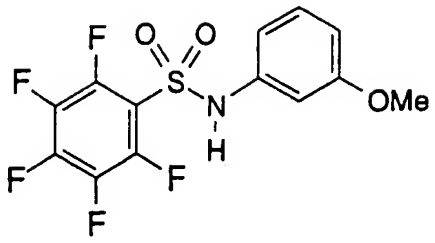
7-Hydroxy-2-pentafluorophenylsulfonamidonaphthalene. The compound was prepared by a protocol similar to that of Example 19 by replacing *p*-phenetidine with 2-amino-7-hydroxynaphthalene. ^{1}H NMR ($CDCl_3$) 8.15 (t, J = 8Hz, 1H), 7.55(d, J=8Hz, 1H), 7.44 (s, 1H), 7.42 (d, J=8Hz, 1H), 7.40 (s, 1H), 6.88ppm (q, J=8Hz, 1H).

Example 23



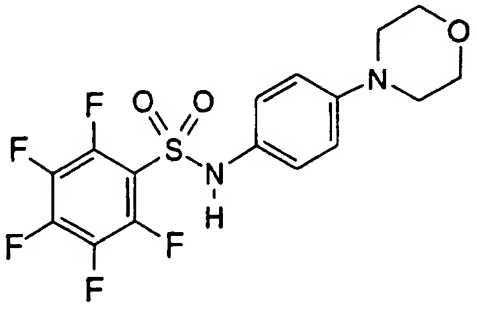
3-Phenoxy-1-pentafluorophenylsulfonamidobenzene. The compound was prepared by a protocol similar to that of Example 19 by replacing *p*-phenetidine with 3-phenoxyaniline. ^{1}H NMR ($CDCl_3$) 7.34 (t, J = 8Hz, 2H), 7.26 (t, J=8Hz, 1H), 7.16 (t, J=8Hz, 1H), 6.94 (d, J=8Hz, 2H), 6.86 (d, J=8Hz, 1H), 6.82 (d, J=8Hz, 1H), 6.74 (s, 1H).

Example 24



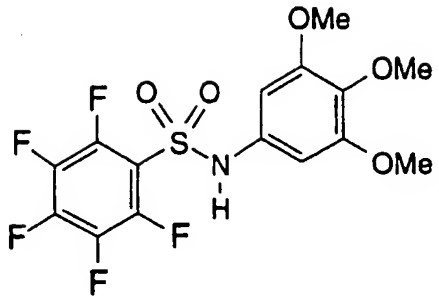
3-Methoxy-1-pentafluorophenylsulfonamidobenzene. The compound was prepared by a protocol similar to that of Example 19 by replacing *p*-phenetidine with 3-methoxyaniline. ^{1}H NMR ($CDCl_3$) 7.20 (d, J = 8Hz, 1H,), 6.95 (s, 1H), 6.78 (d, J=8Hz, 1H,), 6.70 (t, J=8Hz, 1H), 3.79 ppm (s, 1H).

Example 25



4-(1-Morpholino)-1-pentafluorophenylsulfonamidobenzene. The compound was prepared by a protocol similar to that of Example 19 by replacing *p*-phenetidine with 4-(1-morpholino)aniline. ^{1}H NMR ($CDCl_3$) 7.09 (d, J = 8Hz, 2H), 6.85 (d, J=8Hz, 2H), 3.85 (t, J=8Hz, 4H), 3.15ppm (t, J=8Hz, 4H).

Example 26



5-Pentafluorophenylsulfonamido-1,2,3-trimethoxybenzene. The compound was prepared by a protocol similar to that of Example 19 by replacing *p*-phenetidine with 3,4,5-trimethoxyaniline. ^{1}H NMR ($CDCl_3$) 8.14 (s, 1H), 6.46 (s, 2H), 3.69 (s, 6H), 3.59 (s, 3H).

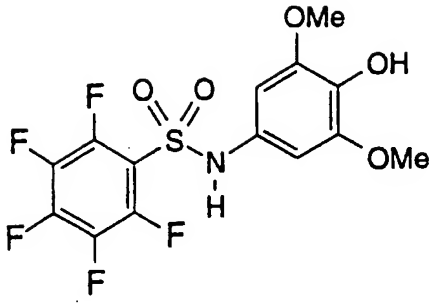
Example 27

1,3-Dimethoxy-2-hydroxy-5-pentafluorophenylsulfonamidobenzene .

1,2-Dihydroxy-3-methoxy-5-pentafluorophenylsulfonamidobenzene.

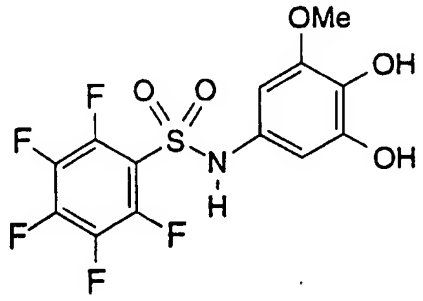
5-Pentafluorophenylsulfonamido-1,2,3-trihydroxybenzene.

1,2,3-Methoxy-5-pentafluorophenylsulfonamidobenzene (269mg, 0.65mmol) was suspended in dry CH_2Cl_2 (5mL) at 0 ^{0}C under nitrogen. To the mixture was added BBr_3 as a 1M solution in CH_2Cl_2 (3.26mmol, 5eq.). The mixture was warmed to ambient temperature and stirred overnight. The reaction mixture was poured over ice (75mL) and extracted 3 times with 30 mL portions of CH_2Cl_2. The organic layer was dried with $MgSO_4$, evaporated, and the residue was subjected to chromatography over silica eluting with 30% (v/v) EtOAc/Hex to afford the three products. The compounds of Examples 28 and 29 were prepared in a manner similar to that described above beginning with the product of Example 20 and treating it with BBr_3.



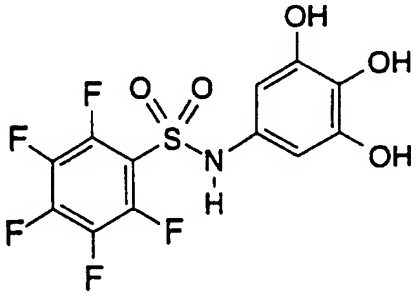
1,3-Dimethoxy-2-hydroxy-5-pentafluorophenylsulfonamidobenzene.

^{1}H NMR ($CDCl_3$) 10.85 (s, 1H), 8.31 (s, 1H), 6.41 (s, 2H), 3.66 ppm (s, 6H).



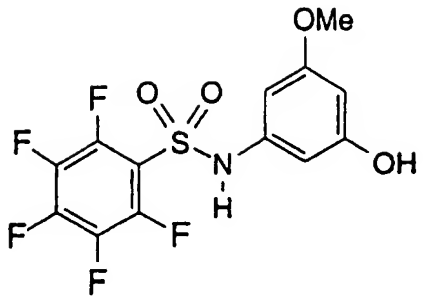
1,2-Dihydroxy-3-methoxy

-5-pentafluorophenylsulfonamidobenzene. ^{1}H NMR ($CDCl_3$) 10.73 (s, 1H), 8.31 (s, 1H), 6.27 (s, 1H). 6.26 (s, 1H), 3.66 ppm (s, 3H).



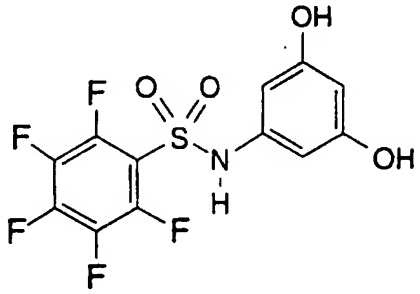
5-Pentafluorophenylsulfonamido-1,2,3-trihydroxybenzene. ^{1}H NMR ($CDCl_3$) 11.0 (s, 1H). 9.03 (s, 2H), 8.06 (s, 1H), 6.13 ppm (s, 2H).

Example 28



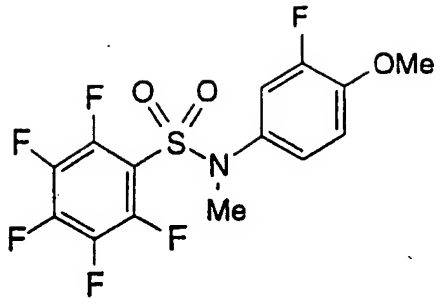
3-Hydroxy-5-methoxy-1-pentafluorophenylsulfonamidobenzene. ^{1}H NMR ($CDCl_3$) 11.2 (s, 1H), 9.63 (s, 1H), 6.23 (s, 1H), 6.21 (s, 1H), 6.08 (s, 1H), 3.63 (s, 3H).

Example 29



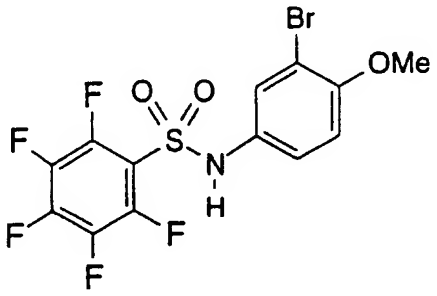
3,5-Dihydroxy-1-pentafluorophenylsulfonamidobenzene. ^{1}H NMR ($CDCl_3$) 7.15 (s, 1H), 6.25 (s, 2H), 6.15 (s, 1H), 5.31 (s, 2H).

Example 30



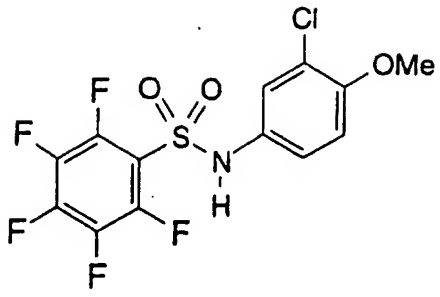
2-Fluoro-1-methoxy-4-(*N*-methylpentafluorophenylsulfonamido)benzene. Prepared using a procedure similar to that of Example 18 replacing 4-(*N*,*N*-dimethylamino)-1-pentafluorophenylsulfonamidobenzene with the appropriate non-substituted sulfonamide (product of Example 7). ^{1}H NMR ($CDCl_3$): 6.97-6.94(m, 2H), 6.89(t, *J*=9Hz, 1H), 3.87(s, 3H), 3.35ppm (t, *J*=1Hz). EI m/z: 385(20, M^+), 154(100). Anal. calcd. for $C_{14}H_9F_6NO_3$: C 43.64, H 2.35, N 3.64. Found C 43.55, H 2.38, N 3.65.

Example 31



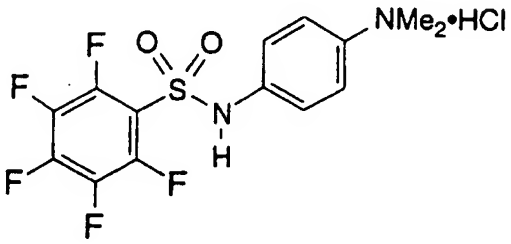
2-Bromo-1-methoxy-4-pentafluorophenylsulfonamidobenzene. ^{1}H NMR ($CDCl_3$): 7.35(d, *J*=3Hz, 1H), 7.15(dd, *J*=9Hz, 3Hz, 1H), 6.97 (s, 1H), 6.81(d, *J*=9Hz, 1H), 3.88 ppm (s, 3H). EI m/z: 433(35, M^+), 202(100). The compound was prepared by a protocol similar to that of example 1 by replacing *N*,*N*-dimethyl-1,4-phenyldiamine dihydrochloride with 3-bromo-4-methoxyaniline.

Example 32



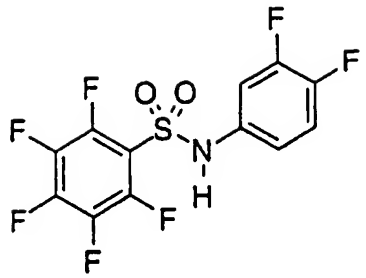
2-Chloro-1-methoxy-4-pentafluorophenylsulfonamidobenzene. ^{1}H NMR ($CDCl_3$): 7.19(d, J=3Hz, 1H), 7.08(dd, J=9Hz, 3Hz, 1H), 7.01 (s, 1H), 6.84(d, J=9Hz, 1H), 3.85 ppm (s, 3H). EI m/z(rel. abundance): 387(10, M^+), 156(100). The compound was prepared by a protocol similar to that of example 1 by replacing *N,N*-dimethyl-1,4-phenyldiamine dihydrochloride with 3-chloro-4-methoxyaniline.

Example 33



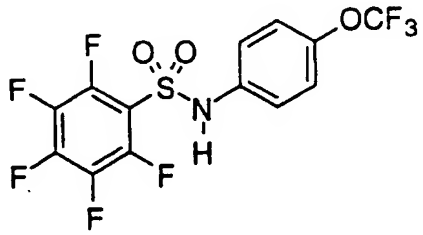
4-(*N,N*-Dimethylamino)-1-pentafluorophenylsulfonamidobenzene hydrochloride. 4-(*N,N*-Dimethylamino)-1-pentafluorophenylsulfonamidobenzene (2g, 5.5mmol) was dissolved in 15mL of diethyl ether at ambient temperature under nitrogen. Gaseous HCl was bubbled into the reaction mixture for 5 min. The mixture was filtered and the resulting solid washed twice with 15mL portions of ice cold diethyl ether to afford the product as a white solid (1.89g, 86% yield). ^{1}H NMR (CD_3OD): 7.62(dd, J=9.0Hz, 1.6Hz, 2H), 7.44(dd, J=9.0Hz, 1.6Hz, 2H), 3.28ppm(s, 6H). FAB m/z: 367(100%, M+H$^+$), 135(90%), 121(45%). Anal. calcd. for $C_{14}H_{13}ClF_5N_2O_2S$: C 41.79, H 3.01, N 6.97, S 7.95. Found C 41.71, H 3.05, N 7.01, S 7.96.

Example 34



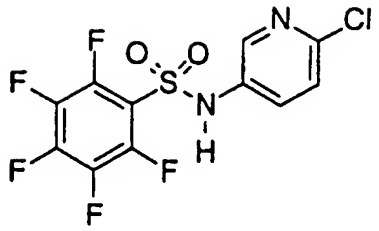
3,4-Difluoro-1-pentafluorophenylsulfonamidobenzene. The compound was prepared in a manner similar to that of example 1 by replacing *N,N*-dimethyl-1,4-phenyldiamine dihydrochloride with 3,4-difluoroaniline. ^{1}H NMR ($CDCl_3$) 7.13 (m. 3H), 6.91ppm (m, 1H). EI, m/z (relative abundance) : 359 (20), 128 (100). Anal. calcd. for $C_{13}H_4F_7NO_2S$: C 40.12. H 1.12, N 3.90. Found: C 40.23, H 1.17, N 3.89.

Example 35



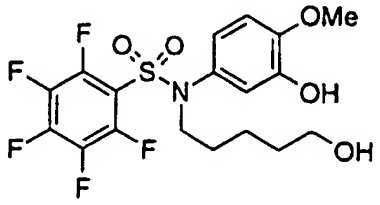
4-Trifluoromethoxy-1-pentafluorophenylsulfonamidobenzene. The compound was prepared in a manner similar to that of example 1 by replacing *N,N*-dimethyl-1,4-phenyldiamine dihydrochloride with 4-(trifluoromethoxy)aniline. ^{1}H NMR ($CDCl_3$) 7.18ppm (m, 4H). EI, m/z (relative abundance) : 407 (20), 176 (100). Anal. calcd. for $C_{13}H_5F_8NO_3S$: C 38.34, H 1.24, N 3.44. Found: C 38.33, H 1.30, N 3.43.

Example 36



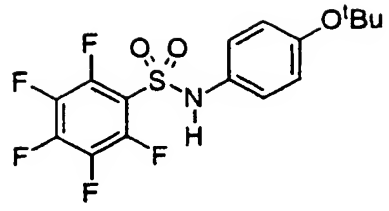
2-Chloro-5-pentafluorophenylsulfonamidopyridine. The compound was prepared in a manner similar to that of example 1 by replacing *N,N*-dimethyl-1,4-phenyldiamine dihydrochloride with 5-amino-2-chloropyridine. H NMR (DMSO-d^6): 8.18 (d, J=2.68 Hz, 1H), 7.64 (dd, J=8.75, 2.89 Hz, 1H), 7.50ppm (d, J=8.75 Hz, 1H). EI m/z 358 (20, M^+), 127 (100). Anal. calcd. for $C_{11}H_4ClF_5N_2O_2S$: C 36.83, H 1.12, N 7.81, S 8.94, Cl 9.90. Found: C 37.00, H 1.16, N 7.78, S 8.98, Cl 10.01. White crystals with M.P.=144-145 ^{0}C.

Example 37



2-Hydroxy-1-methoxy-4-(*N*-(5-hydroxypentyl)-pentafluorophenylsulfonamido)benzene. *N*-(5-hydroxypentyl)-2-hydroxy-1-methoxy-4-aminobenzene was prepared by reductive amination of 5-amino-2-methoxy phenol with glutaric dialdehyde with $NaBH_4$ in MeOH. 2-Hydroxy-1-methoxy-4-(*N*-(5-hydroxypentyl)-pentafluorophenylsulfonamido)benzene was prepared in a manner similar to that of example 1 by replacing *N,N*-dimethyl-1,4-phenyldiamine dihydrochloride with *N*-(5-hydroxypentyl)-2-hydroxy-1-methoxy-4-aminobenzene. ^{1}H NMR ($CDCl_3$): 6.78(d, J=8.6 Hz, 1H), 6.71(dd, J=8.59, 2.48 Hz, 1H), 6.63(d, J=2.48 Hz, 1H), 3.88(s, 3H), 3.7(t, J=6.8 Hz, 2H), 3.6(t, J=6.39 Hz, 2H), 1.5ppm (m, 6H). Anal. calcd. for $C_{18}H_{18}F_5NO_5S$: C 47.47, H 3.98, N 3.08. S 7.04. Found: C 47.47, H 4.04, N 3.11, S 6.97. White crystals with M.P.=118°.

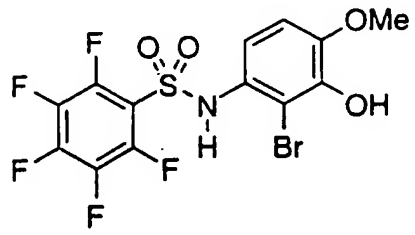
Example 38



4-(1,1-Dimethyl)ethoxy-1-pentafluorophenylsulfonamidobenzene.

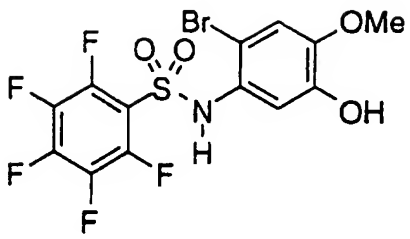
The compound was prepared in a manner similar to example 46 by replacing 3-chloroaniline with 4-*t*-butoxyaniline. 4-*t*-Butoxyaniline was prepared by the method of Day (*J. Med. Chem.* 1975, *18*, 1065). ^{1}H NMR ($CDCl_3$): d 7.07 (m, 2), 6.92 (m, 2), 6.88 (m, 1), 1.31 (s, 9). MS (EI): *m/z* 395 (1. M^+), 339 (28), 108 (100). Anal. Calcd. for $C_{16}H_{14}F_5NO_3S$: C, 48.61; H, 3.57; N, 3.54; S. 8.11. Found: C. 48.53; H. 3.60; N. 3.50; S. 8.02.

Example 39



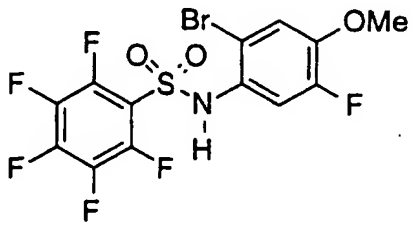
1-Bromo-3-hydroxy-4-methoxy-1-pentafluorophenylsulfonamidobenzene. The compound was prepared by bromination of the compound of example 6 with *N*-bromosuccinimide in dichloromethane. ^{1}H NMR ($CDCl_3$) 7.28 (br s, 1H), 7.21 (d, *J*=9Hz, 1H), 6.80 (d, *J*=9Hz, 1H), 6.05 (s, 1H), 3.89ppm (s, 3H). EI, m/z (relative abundance) : 449 (25), 447 (25), 218 (100), 216 (100). Anal. calcd. for $C_{13}H_8BrF_5NO_4S$: C 34.84, H 1.57, N 3.13, S 7.15. Found: C 34.75, H 1.60, N 3.07, S 7.08.

Example 40



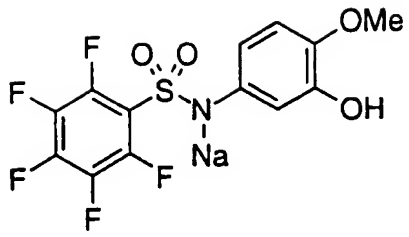
2-Bromo-4-methoxy-5-hydroxy-1-pentafluorophenylsulfonamidobenzene. The compound was prepared by bromination of the compound of example 6 with *N*-bromosuccinimide in dichloromethane. ^{1}H NMR ($CDCl_3$) 7.28 (s, 1H), 7.16 (br s, 1H), 6.91 (s, 1H), 5.63 (s, 1H), 3.85ppm (s, 3H). EI, m/z (relative abundance) : 449 (25), 447 (25), 218 (100), 216 (100). Anal. calcd. for $C_{13}H_8BrF_5NO_4S$: C 34.84, H 1.57, N 3.13, S 7.15. Found: C 34.84, H 1.57, N 3.05, S 7.06.

Example 41



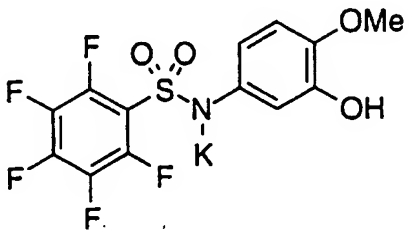
1-Bromo-4-fluoro-5-methoxy-2-pentafluorophenylsulfonamidobenzene. The compound was prepared by bromination of the compound of example 7 with bromine water. ^{1}H NMR ($CDCl_3$): 7.49 (d, J=11.72 Hz, 1H), 7.21 (s, 1H), 7.04 (d, J=8.2 Hz, 1H), 3.84 ppm (s, 3H). EI m/z: 449 (20, M^+), 451 (20), 228 (100), 230 (100). Anal. Calcd. for $C_{13}H_6BrF_6NO_3S$: C 34.69, H 1.34, N 3.11, S 7.12, Br 17.75. Found: C34.76, H 1.29, N 3.05, S 7.12, Br 17.68. White crystals with M.P.= 109 ^{0}C.

Example 42



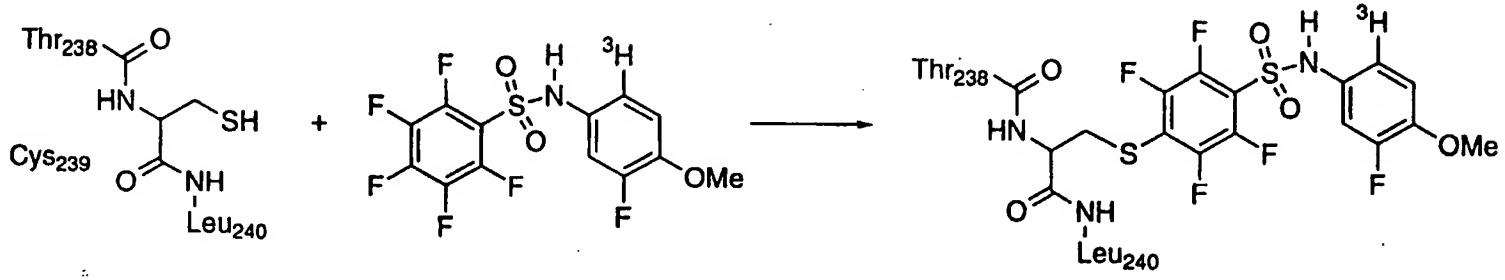
2-Hydroxy-1-methoxy-4-pentafluorophenylsulfonamidobenzene sodium salt. The compound was prepared by treating the compound of example 6 with an equimolar amount of 1N $NaOH_{(aq)}$. The mixture was then lyophilized and the residue recrystallyzed from ethyl acetate/ ether. ^1H NMR (DMSO) 8.40 (s, 1H), 6.57 (d, J=9Hz, 1H), 6.39 (d, J=2Hz, 1H), 6.24 (dd, J=9, 2Hz, 1H), 3.62ppm (s, 3H). Anal. calcd. for $C_{13}H_7F_5NNaO_4S$: C 39.91, H 1.80, N 3.58, Na 5.88, S 8.19. Found: C 39.79, H 1.86, N 3.50, Na 5.78, S 8.07.

Example 43



2-Hydroxy-1-methoxy-4-pentafluorophenylsulfonamidobenzene potassium salt. The compound was prepared in a manner similar to that of example 42 by replacing 1N NaOH with 1N KOH. ^1H NMR (DMSO) 8.30 (br s, 1H), 6.55 (d, J=9Hz, 1H), 6.36 (d, J=2Hz, 1H), 6.25 (dd, J=9, 2Hz, 1H), 3.61ppm (s, 3H). Anal. calcd. for $C_{13}H_7F_5KNO_4S$: C 38.33, H 1.73, N 3.44, S 7.87. Found: C 38.09, H 1.79, N 3.39, S 7.97.

Scheme IV

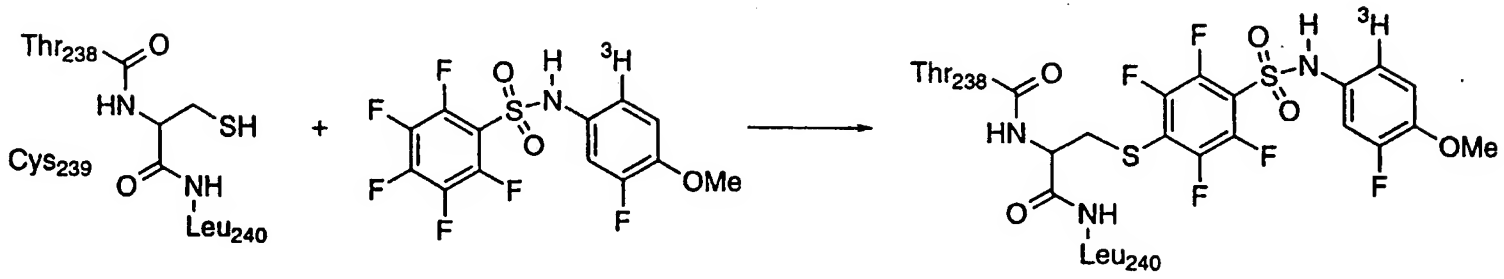


ß1-, ß2-, and ß4-tubulin

[^{3}H]-compound 7

ß1-, ß2-, and ß4-tubulin

Scheme IV

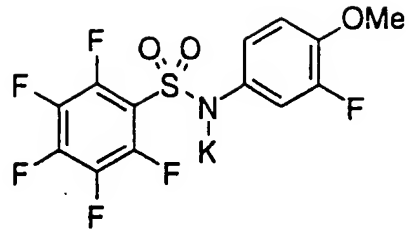


ß1-, ß2-, and ß4-tubulin

[^{3}H]-compound 7

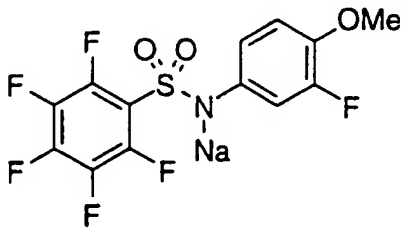
ß1-, ß2-, and ß4-tubulin

Example 44



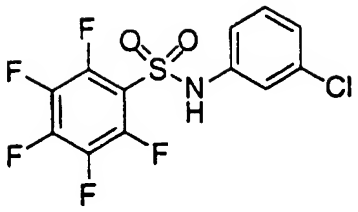
2-Fluoro-1-methoxy-4-pentafluorophenylsulfonamidobenzene potassium salt. The compound was prepared in a manner similar to that of example 43 by replacing the compound from example 6 with example 7. ^{1}H NMR (DMSO) 6.80 (t, J=10Hz, 1H), 6.72 (dd, J=9, 2Hz, 1H), 6.54 (dd, J=9, 2Hz, 1H), 3.68ppm (s, 3H). Anal. calcd. for $C_{13}H_6F_6KNO_3S$: C 38.15, H 1.48, N 3.42, S 7.83. Found: C 38.09, H 1.51, N 3.35, S 7.73. M.P.=202-205 ^{0}C.

Example 45



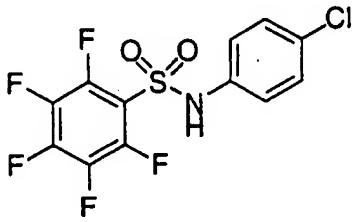
2-Fluoro-1-methoxy-4-pentafluorophenylsulfonamidobenzene sodium salt. The compound was prepared in a manner similar to that of example 44 by replacing 1N KOH with 1N NaOH. ^{1}H NMR (DMSO) 6.80 (t, J=10Hz, 1H), 6.71 (dd, J=9, 2Hz, 1H), 6.53 (dd, J=9, 2Hz, 1H), 3.69ppm (s, 3H). Anal. calcd. for $C_{13}H_6F_6NNaO_3S$: C 39.71, H 1.54, N 3.56, Na 5.85, S 8.15. Found: C 39.56, H 1.62, N 3.49, Na 5.88, S 8.08. M.P. > 250 ^{0}C.

Example 46



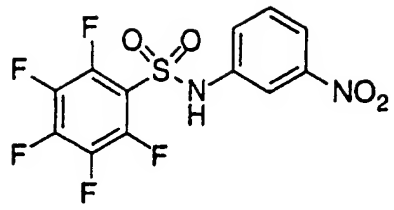
3-Chloro-1-pentafluorophenylsulfonamidobenzene. To a solution of pentafluorophenylsulfonyl chloride (0.15 mL, 1.00 mmol) in MeOH (4 mL) was added 3-chloroaniline (260 mg, 2.04 mmol). After stirring at rt for 1 h, the reaction mixture was concentrated under reduced pressure and the residue was taken up in EtOAc and then filtered through a plug of silica gel. The filtrate was concentrated to give a yellow oil that upon chromatography provided 265 mg (74%) of product. ^{1}H NMR ($CDCl_3$): d 7.28-7.24 (m, 1H), 7.21-7.17 (m, 2H), 7.10-7.08 (m. 1H), 7.07 (s, 1H). MS (EI): *m/z* 357 (42, M^+), 258 (76), 126 (87), 99 (100). Anal. Calcd. for $C_{12}H_5ClF_5NO_2S$: C, 40.30; H, 1.41; N, 3.92; S, 8.96. Found: C, 40.18; H, 1.35; N, 3.84; S, 8.90.

Example 47



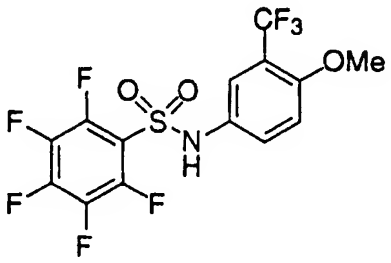
4-Chloro-1-pentafluorophenylsulfonamidobenzene. The compound was prepared in a manner similar to that described in example 46 by replacing 3-chloroaniline with 4-chloroaniline. ^{1}H NMR ($CDCl_3$): d 7.30 (m, 2H), 7.20 (m, 1H), 7.14 (m, 2H). MS (EI): *m/z* 357 (27, M^+), 258 (38), 126 (100), 99 (85). Anal. Calcd. for $C_{12}H_5ClF_5NO_2S$: C. 40.30; H, 1.41; N, 3.92; S, 8.96. Found: C, 40.19; H, 1.37; N, 3.87; S. 8.88.

Example 48



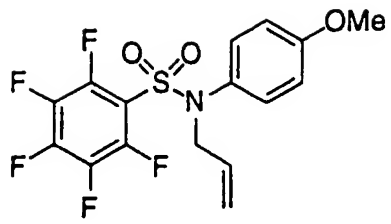
3-Nitro-1-pentafluorophenylsulfonamidobenzene. The compound was prepared in a manner similar to that described in example 46 by replacing 3-chloroaniline with 3-nitroaniline. ^1H NMR ($CDCl_3$): d 8.14 (s, 1H), 8.06-8.03 (m, 2H), 7.66-7.63 (m, 1H), 7.55 (m, 1H). MS (EI): *m/z* 368 (54, M^+), 137 (70), 91 (100). Anal. Calcd. for $C_{12}H_5F_5N_2O_4S$: C. 39.14; H, 1.37; N, 7.61; S, 8.71. Found: C. 39.39; H. 1.45; N. 7.46; S, 8.58.

Example 49



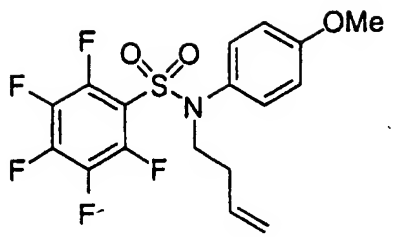
4-Methoxy-1-pentafluorophenylsulfonamido-3-trifluoromethylbenzene. The compound was prepared in a manner similar to that described in example 46 by replacing 3-chloroaniline with 4-methoxy-3-trifluoromethylaniline which was obtained by the hydrogenation of the corresponding nitro compound. White solid, mp 121-123 °C. ^1H NMR ($CDCl_3$): d 7.43-7.37 (m, 2H), 6.96 (d, J = 8.8, 1H), 3.88 (s, 3H). MS (EI): *m/z* 421 (16, M^+), 190 (100). Anal. Calcd. for $C_{14}H_7F_8NO_3S$: C, 39.92; H, 1.67; N, 3.32; S, 7.61. Found: C, 40.17; H, 1.68; N, 3.28; S, 7.67.

Example 50



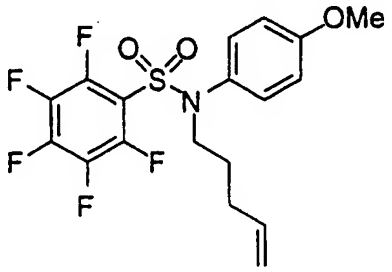
4-Methoxy-1-(*N*-(2-propenyl)pentafluorophenylsulfonamido)benzene. To a solution of 4-methoxy-1-pentafluorophenylsulfonamidobenzene (448 mg, 1.27 mmol) in THF (3 mL) was added triphenylphosphine (333 mg, 1.27 mmol) and allyl alcohol (0.09 mL, 1.27 mmol). Diethylazodicarboxylate (0.20 mL, 1.27 mmol) was added and the mixture was stirred at rt. After 1 h, the reaction mixture was poured onto saturated NaCl (10 mL) and extracted with CH_2Cl_2 (3 x 10 mL). The combined organic extracts were washed with saturated $NaHCO_3$ (10 mL) and dried ($MgSO_4$). Concentration followed by flash chromatography (25:25:1/hexanes:CH_2Cl_2:EtOAc) provided 451 mg (90%) of product as a white solid, mp 59-60 °C. ^1H NMR ($CDCl_3$): d 7.06 (m, 2H), 6.85 (m, 2H), 5.79 (m, 1H), 5.15 (s, 1H), 5.11 (m, 1H), 4.37 (d, J = 6.3, 2H), 3.80 (s, 3H). MS (EI): *m/z* 393 (33, M^+), 162 (100), 134 (66). Anal. Calcd. for $C_{16}H_{11}F_5NO_3S$: C, 48.98; H, 2.83; N, 3.57; S, 8.17. Found: C, 49.13; H, 3.15; N, 3.63; S, 8.15.

Example 51



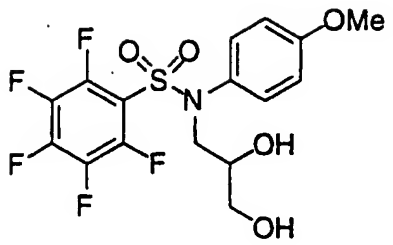
1-(*N*-(3-Butenyl)pentafluorophenylsulfonamido)-4-methoxybenzene. The compound was prepared in a manner similar to that described in example 50 by replacing allyl alcohol with 3-buten-1-ol. White solid, mp 64-66 °C. ^{1}H NMR ($CDCl_3$): d 7.08 (m, 2H), 6.86 (m, 2H), 5.74 (m, 1H), 5.10-5.04 (m. 2H), 3.83 (m, 2H), 3.81 (s, 3H), 2.25 (q, J = 6.9, 2H). MS (EI): *m/z* 407 (13, M^+), 366 (24), 135 (100). Anal. Calcd. for $C_{17}H_{14}F_5NO_3S$: C, 50.13; H, 3.46: N, 3.44; S, 7.87. Found: C, 50.25: H, 3.51; N, 3.43; S, 7.81.

Example 52



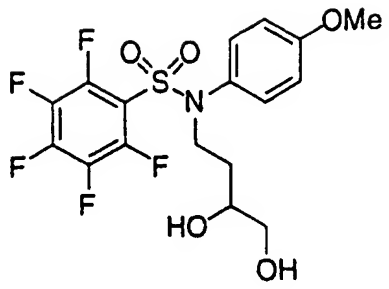
4-Methoxy-1-(*N*-(4-pentenyl)pentafluorophenylsulfonamido)benzene. The compound was prepared in a manner similar to that described in example 50 by replacing allyl alcohol with 4-penten-1-ol. Low melting semi-solid. ^{1}H NMR ($CDCl_3$): d 7.08 (m, 2H), 6.87 (m. 2H), 5.74 (m, 1H), 5.02-4.96 (m, 2H), 3.81 (s, 3H), 3.76 (t,J = 7.04, 2H), 2.11 (q, J = 6.9. 2H), 1.60 (pentet, J = 7.3, 2H). MS (EI): *m/z* 421 (30, M^+), 190 (100). Anal. Calcd. for $C_{18}H_{16}F_5NO_3S$: C, 51.31; H, 3.83; N. 3.32; S, 7.61. Found: C, 51.44; H, 3.89; N. 3.38; S, 7.54.

Example 53



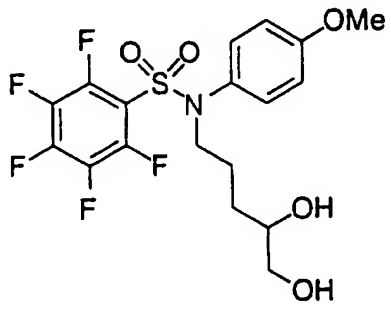
1-(*N*-(2,3-Dihydroxy propyl)pentafluorophenylsulfonamido)-4-methoxybenzene. To a solution of 4-methoxy-1-(*N*-(2-propenyl)pentafluorophenylsulfonamido)benzene (101 mg, 0.26 mmol) in acetone:water (8:1, 1 mL) at rt was added *N*-methylmorpholine *N*-oxide (34.0 mg, 0.29 mmol) and OsO_4 (0.10 mL of 0.16 *M* solution in H_2O, 1.60×10^{-2} mmol). After stirring at rt for 18 h, the reaction mixture was treated with saturated $NaHSO_3$ (5 mL) and allowed to stir at rt. After 1 h, the reaction mixture was poured onto saturated $NaHSO_3$ (5 mL) and extracted with CH_2Cl_2 (3 x 10 mL). The combined organic extracts were dried ($MgSO_4$) and concentrated. Flash chromatography (1:1, 1:2/hexanes:EtOAc) afforded 90 mg (83%) of product as a white solid, mp 130-131 °C. ^1H NMR ($CDCl_3$): d 7.11 (m, 2H), 6.85 (m, 2H), 3.78 (s, 3H), 3.90-3.65 (m, 5H). Anal. Calcd. for $C_{16}H_{13}F_5NO_5S$: C, 45.08; H, 3.07; N, 3.29; S, 7.52. Found: C, 45.09; H, 3.33; N, 3.27; S, 7.46.

Example 54



1-(*N*-(3,4-Dihydroxybutyl)pentafluorophenylsulfonamido)-4-methoxybenzene. The compound was prepared in a manner similar to that described in example 53 by replacing 4-methoxy-1-(*N*-(2-propenyl)pentafluorophenylsulfonamido)benzene with 1-(*N*-(3-butenyl)pentafluorophenylsulfonamido)-4-methoxybenzene. White solid, mp 126-128 °C. ^{1}H NMR ($CDCl_3$): d 7.10 (m, 2H), 6.88 (m, 2H), 4.13 (m, 1H), 3.96 (m, 1H), 3.81 (s, 3H), 3.78-3.73 (m, 1H), 3.64 (dd, 1, *J* = 2.9, 10.7, 1H), 3.47 (dd, *J* = 7.3, 11.2; 1H), 2.67 (bs, 1H), 1.92 (bs, 1H), 1.62 (m, 2H).

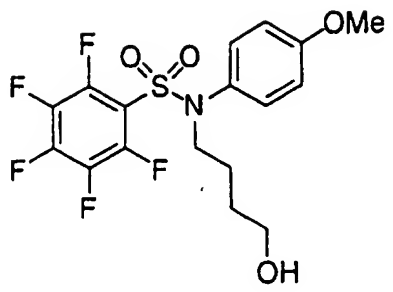
Example 55



1-(*N*-(4,5-Dihydroxypentyl)pentafluorophenylsulfonamido)-4-methoxybenzene. The compound was prepared in a manner similar to that described in example 53 by replacing 4-methoxy-1-(*N*-(2-propenyl)pentafluorophenylsulfonamido)benzene with 4-methoxy-1-(*N*-(4-pentenyl)pentafluorophenylsulfonamido)benzene. White solid, mp 116-118 °C. ^{1}H NMR ($CDCl_3$): d 7.07 (m, 2H), 6.86 (m, 2H), 3.80 (s, 3H), 3.78 (m, 2H), 3.71-3.62 (m, 2H), 3.43 (dd, *J* = 7.5, 10.8; 1H), 1.90 (bs, 2H), 1.66-1.49 (m, 4H). Anal.

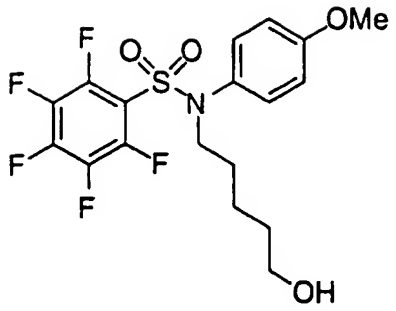
Calcd. for $C_{18}H_{18}F_5NO_5S$: C, 47.48; H, 3.98; N, 3.08; S, 7.04. Found: C, 47.58; H, 3.95; N, 3.06; S, 6.95.

Example 56



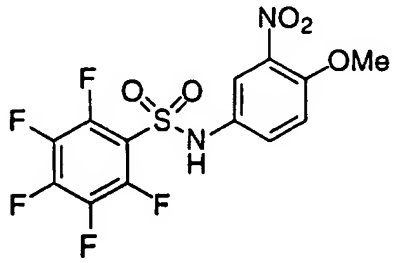
1-(*N*-(4-hydroxybutyl)pentafluorophenylsulfonamido)-4-methoxybenzene. To a solution of 1-(*N*-(3-butenyl)pentafluorophenylsulfonamido)-4-methoxybenzene (410 mg, 1.01 mmol) in THF (6.5 mL) at -78 °C was added BH_3.THF (1.00 mL of a 1 *M* solution in THF, 1.00 mmol). After stirring at -78 °C for 1 h and at 0 °C for 1 h, the reaction mixture was treated with H_2O (20 mL) and sodium perborate (513 mg, 5.14 mmol). After stirring at rt for 2 h, the mixture was poured onto H_2O (20 mL) and extracted with CH_2Cl_2 (3 x 15 mL). The combined organic extracts were washed with sat. NaCl (20 mL) and dried ($MgSO_4$). Concentration followed by chromatography (2:1/hexanes:EtOAc) afforded 270 mg (64%) of product as a white solid. mp 88-90 °C. ^1H NMR ($CDCl_3$): d 7.08 (m, 2H), 6.85 (m, 2H), 3.80 (s, 3H), 3.77 (m, 2H), 3.64 (t, J = 6.0; 2H), 1.63-1.55 (m, 5H), 1.50 (bs, 1H). Anal. Calcd. for $C_{17}H_{16}F_5NO_4S$: C, 48.00; H, 3.79; N, 3.29; S, 7.54. Found: C, 48.08; H, 3.76; N, 3.34; S, 7.46.

Example 57



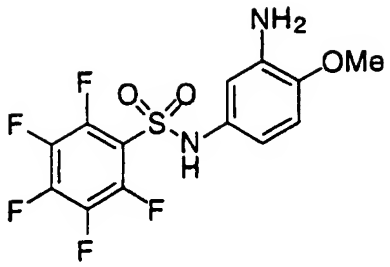
4-Methoxy-1-(*N*-(5-hydroxypentyl)pentafluorophenylsulfonamido)benzene. The compound was prepared in a manner similar to that described in example 56 by replacing 1-(*N*-(3-butenyl)pentafluorophenylsulfonamido)-4-methoxybenzene with 4-methoxy-1-(*N*-(4-pentenyl)pentafluorophenylsulfonamido)benzene. White solid. mp 96-97 °C. ^{1}H NMR ($CDCl_3$): d 7.08 (m, 2H), 6.86 (m, 2H), 3.81 (s, 3H), 3.76 (t, J = 6.8, 2H), 3.62 (t, J = 6.4; 2H), 1.58-1.43 (m, 6H). Anal. Calcd. for $C_{18}H_{18}F_5NO_4S$: C. 49.20; H, 4.13; N, 3.19; S, 7.30. Found: C, 49.11; H, 4.09; N, 3.14; S, 7.19.

Example 58



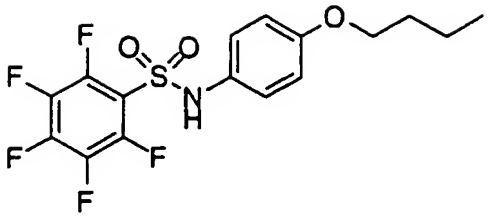
4-Methoxy-3-nitro-1-pentafluorophenylsulfonamidobenzene. The compound was prepared in a manner similar to example 46 by replacing 3-chloroaniline with 4-methoxy-3-nitroaniline which was prepared by the method of Norris (*Aust. J. Chem.* 1971, *24*, 1449). Orange-yellow solid, mp 95-97 °C. ^{1}H NMR ($CDCl_3$): d 7.64 (d, J = 2.7; 1H), 7.51 (dd, J = 2.7, 9.0; 1H), 7.09 (s, 1H), 7.09 (d, J = 9.0; 1H), 3.95 (s, 3H). Anal. Calcd. For $C_{13}H_7F_5N_2O_5S$: C, 39.21; H, 1.77; N, 7.03; S, 8.05. Found: C, 39.19; H, 1.73; N, 6.97; S, 7.95.

Example 59



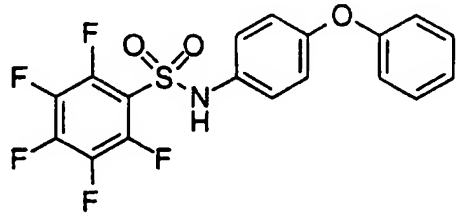
3-Amino-4-methoxy-1-pentafluorophenylsulfonamidobenzene. To a solution of 4-methoxy-3-nitro-1-pentafluorophenylsulfonamidobenzene (627 mg, 1.58 mmol) in ethanol (10 mL) was added 10% Pd/C (51 mg). The resulting mixture was stirred under an atmosphere of hydrogen gas at 1 atm pressure. After 14 h, the mixture was passed through a pad of celite and the filtrate was concentrated to give a solid residue. Silica gel chromatography (2:1, 1:1/hexanes:EtOAc) yielded 542 mg (93%) of product as a white solid, mp 142-143 °C. ^{1}H NMR (DMSO-d_6): 10.64 (s, 1), 6.68 (d, J = 8.4; 1H), 6.44 (d, J = 2.1; 1H), 6.30 (d, J = 2.1, 8.4; 1H), 4.88 (bs, 2H), 3.69 (s, 3H). Anal. Calcd. for $C_{13}H_9F_5N_2O_3S$: C, 42.40; H, 2.46; N, 7.61; S, 8.71. Found: C, 42.29; H, 2.36; N, 7.52; S, 8.60.

Example 60



4-Butoxy-1-pentafluorophenylsulfonamidobenzene. To a solution of pentafluorophenylsulfonyl chloride (203 mg, 0.763 mmol) in MeOH (4 mL) was added 4-butoxyaniline (0.26 mL, 1.53 mmol). After stirring at rt for 1 h, the reaction mixture was poured onto 1 *M* HCl (15 mL) and extracted with CH_2Cl_2 (3 x 10 mL). The combined organic extracts were washed with saturated NaCl (10 mL) and dried ($MgSO_4$). Concentration followed by flash chromatography (25:25:1/hexanes: CH_2Cl_2:EtOAc) provided 189 mg (63%) of product. ^1H NMR ($CDCl_3$): d 7.07 (m, 2H), 6.86 (s, 1H), 6.80 (m, 2H), 3.89 (t, J = 6.5; 2H), 1.73 (m, 2H), 1.46 (m, 2H), 0.95 (t, J = 7.5; 2H). MS (EI): *m/z* 395 (30, M^+), 164 (35), 108 (100). Anal. Calcd. for $C_{16}H_{14}F_5NO_3S$: C, 48.61; H, 3.57; N, 3.54; S, 8.11. Found: C, 48.54; H, 3.53; N, 3.50; S, 8.02.

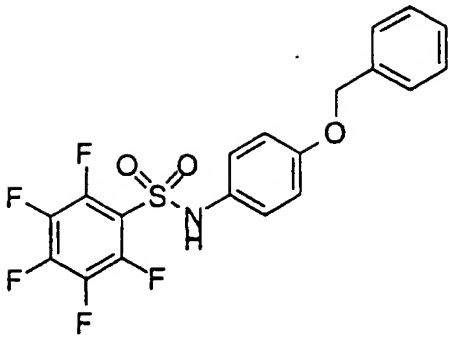
Example 61



1-Pentafluorophenylsulfonamido-4-phenoxybenzene. The compound was prepared in a manner similar to that described in example 60 by replacing 4-butoxyaniline with 4-phenoxyaniline. ^1H NMR ($CDCl_3$): 7.36-7.30 (m, 2H), 7.15-7.10 (m, 3H), 6.99 (s, 1H), 6.98-6.90 (m, 4H). MS (EI): *m/z* 415 (32, M^+), 184 (100), 77 (66). Anal. Calcd. for $C_{18}H_{10}F_5NO_3S$: C, 52.05; H, 2.43; N, 3.27; S, 7.72. Found: C, 51.78; H, 2.45; N, 3.25; S.

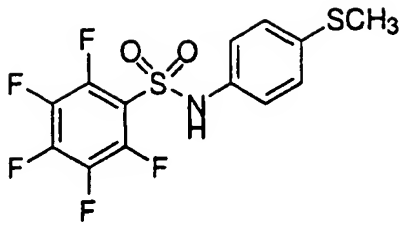
7.53.

Example 62



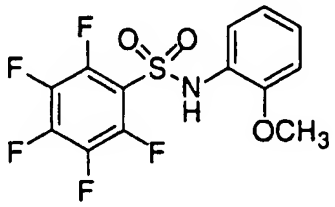
4-Benzyloxy-1-pentafluor ophenylsulfonamidobenzene. The compound was prepared in a manner similar to that described in example 60 by replacing 4-butoxyaniline with 4-benzyloxyaniline. 4-Benzyloxyaniline was obtained from the commercially available hydrochloride salt by treatment with aqueous NaOH. ^{1}H NMR ($CDCl_3$): 7.38-7.37 (m, 4H), 7.36-7.32 (m, 1H), 7.10-7.08 (m, 2H), 7.91-7.88 (m, 2H), 6.78 (s, 1H), 5.01 (s, 1H). MS (EI): *m/z* 429 (19, M^+), 91 (100). Anal. Calcd. for $C_{19}H_{12}F_5NO_3S$: C, 53.14; H, 2.82; N, 3.26; S, 7.45. Found: C, 53.07; H, 2.78; N, 3.21; S, 7.35.

Example 63



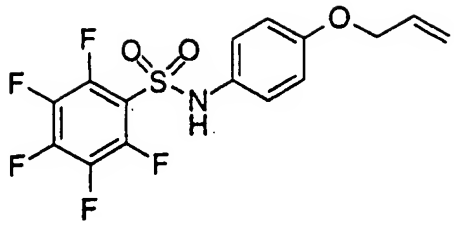
4-Methylmercapto-1-pentafluorophenylsulfonamidobenzene. The compound was prepared in a manner similar to that described in example 60 by replacing 4-butoxyaniline with 4-(methylmercapto)aniline. ^{1}H NMR ($CDCl_3$): 7.17 (m, 2H), 7.09 (m, 2H), 6.89 (m, 1H), 2.44 (s, 3H). MS (EI): *m/z* 369 (24, M^+), 138 (100), 77 (66). Anal. Calcd. for $C_{13}H_8F_5NO_2S_2$: C, 42.28; H, 2.18; N, 3.79; S, 17.36. Found: C, 42.20; H, 2.21; N, 3.72; S, 17.28.

Example 64



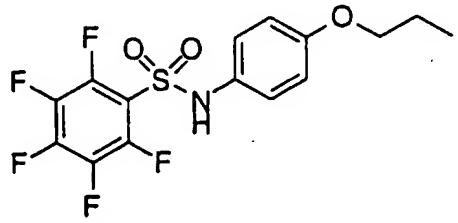
2-Methoxy-1-pentafluorophenylsulfonamidobenzene. The compound was prepared in a manner similar to that described in example 60 by replacing 4-butoxyaniline with *o*-anisidine. ^{1}H NMR ($CDCl_3$): d 7.54 (dd, J = 1.5, 8.0; 1H), 7.13 (dt, J = 1.5, 8.0; 1H), 6.94 (dt, J = 1.2, 8.0; 1H), 6.84 (dd, J = 1.2, 8.0; 1H), 3.79 (s, 3H). MS (EI): *m/z* 353 (82, M^+), 122 (100), 94 (95). Anal. Calcd. for $C_{13}H_8F_5NO_3S$: C, 44.19; H, 2.28; N, 3.97; S, 9.06. Found: C, 44.10; H, 2.26; N, 3.92; S, 9.03.

Example 65



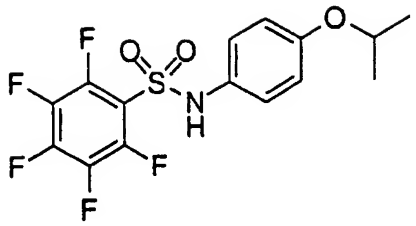
4-Allyloxy-1-pentafluorophenylsulfonamidobenzene. The compound was prepared in a manner similar to that described in example 60 by replacing 4-butoxyaniline with 4-allyloxyaniline. 4-Allyloxyaniline was prepared by the method of Butera (*J. Med. Chem.* 1991, *34*, 3212). ^{1}H NMR ($CDCl_3$): 7.08 (m, 2H), 6.87 (m, 1H), 6.82 (m, 2H), 6.04-5.94 (m, 1H), 5.39-5.34 (m, 1H), 5.29-5.25 (m, 1H), 4.48-4.46 (m, 2H). MS (EI): *m/z* 379 (11, M^+). 148 (32), 41 (100). Anal. Calcd. for $C_{15}H_{10}F_5NO_3S$: C, 47.50; H, 2.66; N, 3.96; S, 8.45. Found: C, 47.53; H, 2.68; N, 3.62; S, 8.37.

Example 66



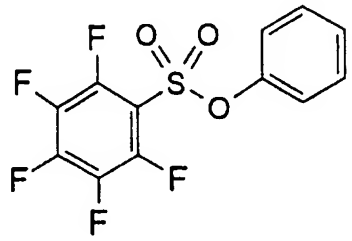
1-Pentafluorophenylsulfonamido-4-propoxybenzene. The compound was prepared in a manner similar to that described in example 60 by replacing 4-butoxyaniline with 4-propoxyaniline. 4-Propoxyaniline was obtained by catalytic hydrogenation of 4-allyloxynitrobenzene. 4-Allyloxynitrobenzene was prepared by the method of Butera (*J. Med. Chem.* 1991, *34*, 3212). ^{1}H NMR ($CDCl_3$): 7.09 (m, 2H), 6.82 (m, 2H), 6.78 (m, 1H), 3.87 (t, J = 6.5; 2H), 1.78 (m, 2H), 1.02 (t, J = 7.4; 3H). MS (EI): *m/z* 381 (20, M^+), 150 (40), 108 (100). Anal. Calcd. for $C_{15}H_{12}F_5NO_3S$: C, 47.25; H, 3.17; N, 3.67; S, 8.41. Found: C, 47.01; H, 3.20; N, 3.61; S, 8.31.

Example 67



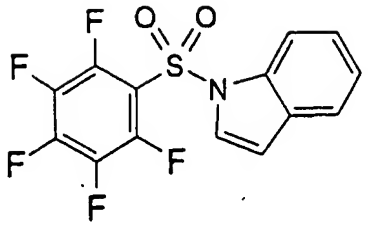
4-(1-Methyl)ethoxy-1-pentafluorophenylsulfonamidobenzene. The compound was prepared in a manner similar to that described in example 60 by replacing 4-butoxyaniline with 4-isopropoxyaniline. 4-Isopropoxyaniline was prepared from 4-fluoronitrobenzene in analogy to the method of Day (*J. Med. Chem.* 1975, 18, 1065). ^{1}H NMR ($CDCl_3$): 7.08 (m, 2H), 7.00 (s, 1H), 6.81 (m, 2H), 4.48 (heptet, J = 6.1: 1H), 1.30 (d, J = 6.04; 6H). MS (EI): *m/z* 381 (7, M^+), 339 (8), 108 (100). Anal. Calcd. for $C_{15}H_{12}F_5NO_3S$: C, 47.25; H, 3.17; N, 3.67; S, 8.41. Found: C, 47.08; H, 3.18; N, 3.60; S, 8.34.

Example 68



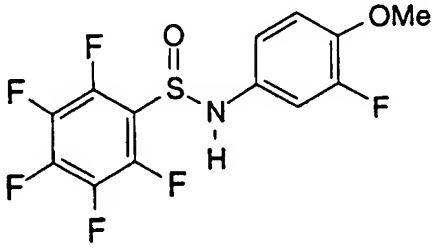
1-Pentafluorophenylsulfonyloxybenzene. To a stirred solution of phenol (0.068g, 0.729mmol) in dimethylformamide (3.65 mL) at 25 ^{0}C is added pentafluorophenyl sulfonyl chloride (0.135mL, 0.911mmol), followed by sodium carbonate (0.116g, 1.09mmol), and the reaction mixture is stirred for 18 hours. The reaction mixture is diluted with ethyl acetate (50mL), washed with 20% ammonium chloride (2 x 20mL), and saturated sodium chloride (2 x 20mL). The organic layer is dried (sodium sulfite), and the ethyl acetate removed under vacuum. Column chromatography (3/1 ethyl acetate/hexane) yields the title compound.

Example 69



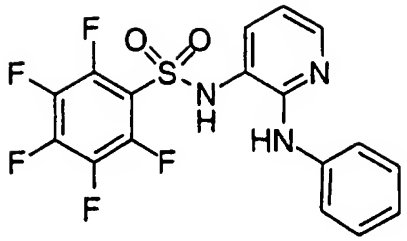
1-Pentafluorophenylsulfonylindole. To a stirred solution of indole (0.085g, 0.729mmol) in dimethylformamide (3.65 mL) at 25 ^{0}C is added pentafluorophenyl sulfonyl chloride (0.135mL, 0.911mmol), followed by sodium carbonate (0.116g, 1.09mmol), and the reaction mixture is stirred for 18 hours. The reaction mixture is diluted with ethyl acetate (50mL), washed with 20% ammonium chloride (2 x 20mL), and saturated sodium chloride (2 x 20mL). The organic layer is dried (sodium sulfite), and the ethyl acetate removed under vacuum. Column chromatography (3/1 ethyl acetate/hexane) yields the title compound.

Example 70



2-Fluoro-1-methoxy-4-pentafluorophenylsulfinamidobenzene. To 3-fluoro-*p*-anisidine (3g, 21.2mmol) suspended in THF (50mL) with pyridine (1.84g, 23.3mmol) at 0 ^{0}C under argon is added dropwise pentafluorophenylsulfinyl chloride (5.3g, 21.2mmol). The reaction mixture is stirred for 30 min. at 0 ^{0}C and allowed to warm to ambient temperature. The reaction mixture is strirred at room temperature and followed by TLC. After the reaction is completed the mixture is diluted with ethyl acetate and the reaction quenched with water. The layers are separated and the aqueous layer extracted twice with ethyl acetate. The organic layers are combined and dried with brine and with Na_2SO_4. The solvent is evaporated and the residue purified by chromatography on silica to give the title compound.

Example 71



2-Anilino-3-pentafluorophenylsulfonamidopyridine. To a solution of pentafluorophenylsulfonyl chloride (863 mg, 3.24 mmol) in pyridine (9 mL) at rt was added 3-amino-2-analinopyridine (600 mg, 3.24 mmol). After stirring at rt overnight the reaction mixture was concentrated at reduced pressure and the residue partitioned between 1 M Hcl (50 mL) and CH2Cl2 (50 mL). The organic extract was dried and concentrated to give an oil which was purified by MPLC to give 377 mg (28%) of product as an orange solid. H^1 NMR ($CDCl_3$): 8.50 (bs, 1H), 7.80 (d, J=5.1, 1H), 7.61 (d, J=8.0, 1H), 7.32 (t, J=8.0, 2H), 7.25 (d, J=8.0, 2H), 7.11 (t, J=7.3, 1H), 6.80 (dd, J=5.6, 7.7, 1H), 4.20 (bs, 1H). MS (FAB): *m/z* 438 (M+Na), 416 (M+H).

Example 72

4-[^{3}H]-1-Fluoro-2-methoxy-5-pentafluorosulfonamidobenzene.

A solution of 1-bromo-4-fluoro-5-methoxy-2-pentafluorophenylsulfonamidobenzene (27.8 mg, 0.058 mmol; prepared in Example 41) in ethyl acetate (2 mL) was treated with 100 mg of 10% palladium on charcoal. The air in the reaction vessel was evacuated and replaced with tritium gas. After 2 h of stirring at room temperature, the catalyst was filtered, the solvent was evaporated, and the crude product purified by preparative thin layer chromatography (TLC) using dichloromethane as the eluent. The sample purity was characterized by HPLC using a Microsorb silica (250x4.6mm) 5 mm column and 15% ethyl acetate/hexane as the mobile phase. The elution of material was detected using a UV detector at 254 nm and a Beta Ram detector. The chemical purity of this material was determined to be 100%, and the radiochemical purity was 99.3%. The specific activity of this material was Ci/mmol.

Example 73

Compounds were evaluated for their ability to inhibit in vitro the growth of HeLa cells, an immortal cell line derived from a human cervical carcinoma commonly used to evaluate the cytotoxicity of potential therapeutic agents. The following data reflect the cytotoxicity of selected examples of the present invention. The values given represent the concentration of test compound required to inhibit by 50% the uptake of Alamar Blue (Biosource International, Camarillo, CA) by HeLa cell cultures, which correlates directly with the overall levels of cellular metabolism in the culture, and is generally accepted as an appropriate marker of cell growth. The test was conducted according to the method of S.A. Ahmed et al. (1994) J. Immunol. Methods 170: 211-224. The following selected examples display potent cytotoxic activity in this assay, with IC_{50} values ranging from less than 0.05 μM to 10 μM.

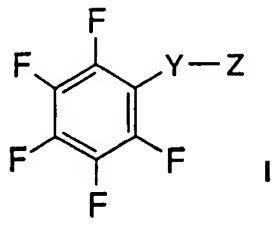
Compound	IC50 (μM)
Example 1	< 0.05
Example 2	0.15
Example 3	1.5
Example 4	10
Example 6	< 0.05
Example 7	< 0.05
Example 8	< 0.05
Example 9	1
Example 12	0.15
Example 15	1
Example 17	10
Example 25	10
Example 30	1.5
Example 31	0.5
Example 32	0.1

All publications and patent applications cited in this specification are herein incorporated by reference as if each individual publication or patent application were specifically and

individually indicated to be incorporated by reference. Although the foregoing invention has been described in some detail by way of illustration and example for purposes of clarity of understanding, it will be readily apparent to those of ordinary skill in the art in light of the teachings of this invention that certain changes and modifications may be made thereto without departing from the spirit or scope of the appended claims.

WHAT IS CLAIMED IS:

1. A pharmaceutical composition comprising a pharmaceutically acceptable excipient and a compound of formula I:



I

or a pharmaceutically acceptable salt thereof, wherein:

Y is -S(O)- or -$S(O)_2$-; and

Z is -NR^1R^2 or -OR^3; wherein R^1 and R^2 are independently selected from

hydrogen,

substituted or unsubstituted (C1-C10)alkyl,

substituted or unsubstituted (C1-C10)alkoxy,

substituted or unsubstituted (C3-C6)alkenyl,

substituted or unsubstituted (C2-C6)heteroalkyl,

substituted or unsubstituted (C3-C6)heteroalkenyl,

substituted or unsubstituted (C3-C6)alkynyl,

substituted or unsubstituted (C3-C8)cycloalkyl,

substituted or unsubstituted (C5-C7)cycloalkenyl,

substituted or unsubstituted (C5-C7)cycloalkadienyl,

substituted or unsubstituted aryl,

substituted or unsubstituted aryloxy,

substituted or unsubstituted aryl-(C3-C8)cycloalkyl,

substituted or unsubstituted aryl-(C5-C7)cycloalkenyl,

substituted or unsubstituted aryloxy-(C3-C8)cycloalkyl,

substituted or unsubstituted aryl-(C1-C4)alkyl,

substituted or unsubstituted aryl-(C1-C4)alkoxy,

substituted or unsubstituted aryl-(C1-C4)heteroalkyl,

substituted or unsubstituted aryl-(C3-C6)alkenyl,

substituted or unsubstituted aryloxy-(C1-C4)alkyl,

substituted or unsubstituted aryloxy-(C2-C4)heteroalkyl,

substituted or unsubstituted heteroaryl,

substituted or unsubstituted heteroaryloxy,

substituted or unsubstituted heteroaryl-(C1-C4)alkyl,

substituted or unsubstituted heteroaryl-(C1-C4)alkoxy,

substituted or unsubstituted heteroaryl-(C1-C4)heteroalkyl,

substituted or unsubstituted heteroaryl-(C3-C6)alkenyl,

substituted or unsubstituted heteroaryloxy-(C1-C4)alkyl, and

substituted or unsubstituted heteroaryloxy-(C2-C4)heteroalkyl,

wherein R^1 and R^2 may be connected by a linking group E to give a substituent of the formula

wherein E represents a bond, (C1-C4) alkylene, or (C1-C4) heteroalkylene, and the ring formed by R^1, E, R^2 and the nitrogen atom contains no more than 8 atoms;

and where R^3 is a substituted or unsubstituted aryl or heteroaryl group, wherein said compound I has pharmacological activity.

2. The composition of claim 1, wherein, in the compound of formula I,

Y is SO_2 and

Z is NR^1R^2; wherein R^2 is optionally substituted aryl or optionally substituted heteroaryl.

3. The composition of claim 2, wherein R^1 is hydrogen or lower alkyl, R^2 is optionally substituted phenyl or optionally substituted pyridyl, and there is no linking group E between R^1 and R^2.

4. The composition of claim 3, wherein R^1 is hydrogen or methyl and R^2 is substituted phenyl, wherein the substituents on R^2, ranging in number from one to four, are

independently chosen from lower alkyl, hydroxy, lower alkoxy, amino optionally substituted with one or two lower alkyls, optionally substituted arylamino, optionally substituted heteroarylamino, optionally substituted phenoxy, and halogen.

5. The composition of claim 4, wherein R^1 is hydrogen and R^2 is substituted phenyl, wherein the substituents on R^2 are independently chosen from amino, (lower)alkylamino, and di(lower)alkylamino, and are located at one or more of positions 3- and 4- of the phenyl ring, in relation to the sulfonamido group.

6. The composition of claim 5, wherein the compound is
4-(N,N-Dimethylamino)-1-pentafluorophenylsulfonamidobenzene,
4-(*N,N*-Diethylamino)-1-pentafluorophenylsulfonamidobenzene,
3-(*N,N*-Dimethylamino)-1-pentafluorophenylsulfonamidobenzene,
4-Amino-1-pentafluorophenylsulfonamidobenzene, or
4-(*N,N*-Dimethylamino)-1-pentafluorophenylsulfonamidobenzene hydrochloride.

7. The composition of claim 6, wherein the compound is
4-(*N,N*-Dimethylamino)-1-pentafluorophenylsulfonamidobenzene.

8. The composition of claim 2. wherein the compound is
Pentafluorophenylsulfonamidobenzene.

9. The composition of claim 3, wherein R^1 is hydrogen, and R^2 is phenyl substituted at positions 3- and 4-, in relation to the sulfonamido group, with a divalent moiety that forms a 5- or 6- membered ring together with carbons 3- and 4- of the phenyl ring.

10. The composition of claim 9, wherein the divalent moiety is: $-OCH_2CH_2O-$, $-OCH_2O-$, -C=CNH-, or -C=NNH-.

11. The composition of claim 10, wherein the compound is
1,2-Ethylenedioxy-4-pentafluorophenylsulfonamidobenzene,

1,2-Methylenedioxy-4-pentafluorophenylsulfonamidobenzene,
5-Pentafluorophenylsulfonamidoindazole, or
5-Pentafluorophenylsulfonamidoindole.

12. The composition of claim 4, wherein R^1 is hydrogen, and the substituents on R^2 are independently selected from halogen, hydroxy, lower alkyl, lower alkoxy, amino, (lower)alkylamino, and di(lower)alkylamino.

13. The composition of claim 12, wherein the substituents on R^2 are independently selected from bromo, chloro, fluoro, hydroxy, methoxy, ethoxy, amino, and dimethylamino.

14. The composition of claim 13, wherein the substituents on R^2 are independently selected from bromo, chloro, fluoro, hydroxy, methoxy, and ethoxy.

15. The composition of claim 12, wherein the substituents on R^2 are at one or more of positions 3- and 4- of the phenyl ring, in relation to the sulfonamido group.

16. The composition of claim 15, wherein R^2 is monosubstituted phenyl.

17. The composition of claim 16, wherein the compound is
4-Methoxy-1-pentafluorophenylsulfonamidobenzene,
3-Hydroxy-1-pentafluorophenylsulfonamidobenzene,
4-Hydroxy-1-pentafluorophenylsulfonamidobenzene,
4-Ethoxy-1-pentafluorophenylsulfonamidobenzene,
3-Ethoxy-1-pentafluorophenylsulfonamidobenzene,
3-Phenoxy-1-pentafluorophenylsulfonamidobenzene,
3-Methoxy-1-pentafluorophenylsulfonamidobenzene, or
4-*tert*-Butoxy-1-pentafluorophenylsulfonamidobenzene.

18. The composition of claim 16, wherein the compound is
3-Chloro-1-pentafluorophenylsulfonamidobenzene, or

4-Chloro-1-pentafluorophenylsulfonamidobenzene.

19. The composition of claim 15, wherein R^2 is disubstituted phenyl.

20. The composition of claim 19, wherein the compound is
1,2-Dimethoxy-4-pentafluorophenylsulfonamidobenzene,
2-Hydroxy-1-methoxy-4-pentafluorophenylsulfonamidobenzene,
1,2-Dihydroxy-4-pentafluorophenylsulfonamidobenzene,
2-Hydroxy-1-methoxy-4-pentafluorophenylsulfonamidobenzene, monosodium salt, or
2-Hydroxy-1-methoxy-4-pentafluorophenylsulfonamidobenzene, monopotassium salt.

21. The composition of claim 19, wherein the compound is
2-Fluoro-1-methoxy-4-pentafluorophenylsulfonamidobenzene,
2-Bromo-1-methoxy-4-pentafluorophenylsulfonamidobenzene,
2-Chloro-1-methoxy-4-pentafluorophenylsulfonamidobenzene,
2-Fluoro-1-methoxy-4-pentafluorophenylsulfonamidobenzene, sodium salt, or
2-Fluoro-1-methoxy-4-pentafluorophenylsulfonamidobenzene, potassium salt.

22. The composition of claim 20, wherein the compound is
2-Hydroxy-1-methoxy-4-pentafluorophenylsulfonamidobenzene.

23. The composition of claim 20, wherein the compound is
2-Hydroxy-1-methoxy-4-pentafluorophenylsulfonamidobenzene, monosodium salt.

24. The composition of claim 21, wherein the compound is
2-Fluoro-1-methoxy-4-pentafluorophenylsulfonamidobenzene.

25. The composition of claim 21, wherein the compound is
2-Fluoro-1-methoxy-4-pentafluorophenylsulfonamidobenzene, sodium salt.

26. The composition of claim 21, wherein the compound is

2-Fluoro-1-methoxy-4-pentafluorophenylsulfonamidobenzene, potassium salt.

27. The composition of claim 12, wherein R^2 is a trisubstituted phenyl.

28. The composition of claim 21, wherein the compound is 2-Bromo-1-methoxy-4-pentafluorophenylsulfonamidobenzene, or 2-Chloro-1-methoxy-4-pentafluorophenylsulfonamidobenzene.

29. The composition of claim 12, wherein the compound is 1,2-Dimethyl-4-pentafluorophenylsulfonamidobenzene.

30. The composition of claim 1, wherein in the compound of formula I,

Y is SO_2 and

Z is NR^1R^2, where R^1 is hydrogen or lower alkyl, and R^2 is an unsubstituted or optionally substituted naphthyl group.

31. The composition of claim 30, wherein the compound is 7-Hydroxy-2-pentafluorophenylsulfonamidonaphthalene.

32. The composition of claim 4, wherein R^2 is a phenyl group substituted by phenoxy or optionally substituted phenoxy.

33. The composition of claim 32, wherein the compound is 3-Phenoxy-1-pentafluorophenylsulfonamidobenzene.

34. The composition of claim 3, wherein R^2 is a phenyl ring substituted by a heterocyclic group at the 4- position, in relation to the sulfonamido group.

35. The composition of claim 17, wherein the compound is 4-Methoxy-1-pentafluorophenylsulfonamidobenzene.

36. The composition of claim 2, wherein R^1 and R^2 are covalently joined in a moiety that forms a 5- or 6- membered heterocyclic ring with the nitrogen atom of NR^1R^2.

37. The composition of claim 36, wherein R^1 is a -CH=CH- group linked to the 2-position of the R^2 phenyl group, in relation to the sulfonamido group, forming an optionally substituted indole.

38. The composition of claim 37, wherein the compound is 1-pentafluorophenylsulfonylindole.

39. The composition of claim 36, wherein R^1 is a $-(CH_2)_3-$ group linked to the 2- position of the R^2 phenyl group, in relation to the sulfonamido group, forming an optionally substituted 1,2,3,4-tetrahydroquinoline.

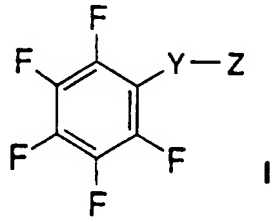
40. The composition of claim 39, wherein the compound is 1-pentafluorophenylsulfonyl-1,2,3,4-tetrahydroquinoline.

41. The composition of claim 2, wherein R^1 is an optionally substituted (C2-C10)alkyl or optionally substituted (C2-C6)heteroalkyl.

42. The composition of claim 41, wherein the compound is
2-Hydroxy-1-methoxy-4-[N-(5-hydroxypent-1-yl)pentafluorophenyl-sulfonamido]benzene,
4-Methoxy-1-[N-(2-propenyl)pentafluorophenylsulfonamido]benzene,
4-Methoxy-1-[N-(4-pentenyl)pentafluorophenylsulfonamido]benzene,
1-[N-(2,3-Dihydroxypropyl) pentafluorophenylsulfonamido]-4-methoxybenzene,
1-[N-(3,4-Dihydroxybutyl)pentafluorophenylsulfonamido]-4-methoxybenzene,
1-[N-(4,5-Dihydroxypentyl)pentafluorophenylsulfonamido]-4-methoxybenzene,
1-[N-(4-hydroxybutyl)pentafluorophenylsulfonamido]-4-methoxybenzene, or
4-Methoxy-1-[N-(5-hydroxypentyl)pentafluorophenylsulfonamido]benzene.

43. A method of treating or preventing a disease state characterized by an abnormal or

undesired level of cell proliferation, which method comprises administering to a mammalian subject in need thereof a therapeutically effective amount of a composition containing a compound of formula I



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or a pharmaceutically acceptable salt thereof, wherein:

Y is -S(O)- or -$S(O)_2$-;

Z is -NR^1R^2 or -OR^3; where R^1 and R^2 are independently selected from

hydrogen,

substituted or unsubstituted (C1-C10)alkyl,

substituted or unsubstituted (C1-C10)alkoxy,

substituted or unsubstituted (C3-C6)alkenyl,

substituted or unsubstituted (C2-C6)heteroalkyl,

substituted or unsubstituted (C3-C6)heteroalkenyl,

substituted or unsubstituted (C3-C6)alkynyl,

substituted or unsubstituted (C3-C8)cycloalkyl,

substituted or unsubstituted (C5-C7)cycloalkenyl,

substituted or unsubstituted (C5-C7)cycloalkadienyl,

substituted or unsubstituted aryl,

substituted or unsubstituted aryloxy,

substituted or unsubstituted aryl-(C3-C8)cycloalkyl,

substituted or unsubstituted aryl-(C5-C7)cycloalkenyl,

substituted or unsubstituted aryloxy-(C3-C8)cycloalkyl,

substituted or unsubstituted aryl-(C1-C4)alkyl,

substituted or unsubstituted aryl-(C1-C4)alkoxy,

substituted or unsubstituted aryl-(C1-C4)heteroalkyl,

substituted or unsubstituted aryl-(C3-C6)alkenyl,

substituted or unsubstituted aryloxy-(C1-C4)alkyl,

substituted or unsubstituted aryloxy-(C2-C4)heteroalkyl,

substituted or unsubstituted heteroaryl,

substituted or unsubstituted heteroaryloxy,

substituted or unsubstituted heteroaryl-(C1-C4)alkyl,

substituted or unsubstituted heteroaryl-(C1-C4)alkoxy,

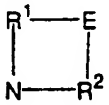
substituted or unsubstituted heteroaryl-(C1-C4)heteroalkyl,

substituted or unsubstituted heteroaryl-(C3-C6)alkenyl,

substituted or unsubstituted heteroaryloxy-(C1-C4)alkyl, and

substituted or unsubstituted heteroaryloxy-(C2-C4)heteroalkyl,

wherein R^1 and R^2 may be connected by a linking group E to give a substituent of the formula



wherein E represents a bond, (C1-C4) alkylene, or (C1-C4) heteroalkylene, and the ring formed by R^1, E, R^2 and the nitrogen contains no more than 8 atoms;

and where R^3 is optionally substituted aryl or optionally substituted heteroaryl.

44. The method of claim 43 wherein, in the compound of formula I.

Y is SO_2, and

Z is NR^1R^2; where R^2 is optionally substituted aryl or optionally substituted heteroaryl.

45. The method of claim 44, wherein R^1 is hydrogen or lower alkyl, R^2 is optionally substituted phenyl, and there is no linking group E between R^1 and R^2.

46. The method of claim 45, wherein R^1 is hydrogen or methyl, and the substituents on R^2 are independently chosen from lower alkyl, hydroxy, lower alkoxy, amino, amino optionally substituted with one or two lower alkyls, optionally substituted arylamino, optionally substituted heteroarylamino, optionally substituted phenoxy, and halogen.

47. The method of claim 46, wherein the compound is chosen from:

4-(N,N-Dimethylamino)-1-pentafluorophenylsulfonamidobenzene,

3-(N,N-Dimethylamino)-1-pentafluorophenylsulfonamidobenzene,

1,2-Ethylenedioxy-4-pentafluorophenylsulfonamidobenzene,

1,2-Methylenedioxy-4-pentafluorophenylsulfonamidobenzene,

1,2-Dimethoxy-4-pentafluorophenylsulfonamidobenzene,

2-Hydroxy-1-methoxy-4-pentafluorophenylsulfonamidobenzene,

2-Fluoro-1-methoxy-4-pentafluorophenylsulfonamidobenzene,

4-Methoxy-1-pentafluorophenylsulfonamidobenzene,

3-Hydroxy-1-pentafluorophenylsulfonamidobenzene,

4-Hydroxy-1-pentafluorophenylsulfonamidobenzene,

1,2-Dimethyl-4-pentafluorophenylsulfonamidobenzene,

4-(N,N-Diethylamino)-1-pentafluorophenylsulfonamidobenzene,

4-Amino-1-pentafluorophenylsulfonamidobenzene,

Pentafluorophenylsulfonamidobenzene,

5-Pentafluorophenylsulfonamidoindazole,

5-Pentafluorophenylsulfonamidoindole,

4-(N,N-Dimethylamino)-1-(N-methylpentafluorophenylsulfonamido)benzene,

4-(N,N-Dimethylamino)-1-(pentafluorophenylsulfonamido)benzene,

1,2-Dihydroxy-4-pentafluorophenylsulfonamidobenzene,

4-Ethoxy-1-pentafluorophenylsulfonamidobenzene,

3,5-Dimethoxy-1-pentafluorophenylsulfonamidobenzene,

3-Ethoxy-1-pentafluorophenylsulfonamidobenzene,

7-Hydroxy-2-pentafluorophenylsulfonamidonaphthalene,

3-Phenoxy-1-pentafluorophenylsulfonamidobenzene,

3-Methoxy-1-pentafluorophenylsulfonamidobenzene,

4(1-Morpholino)-1-pentafluorophenylsulfonamidobenzene,

5-Pentafluorophenylsulfonamido-1,2,3-trimethoxybenzene,

2-Hydroxy-1,3-methoxy-5-pentafluorophenylsulfonamidobenzene,

1,2-Dihydroxy-3-methoxy-5-pentafluorophenylsulfonamidobenzene,

5-Pentafluorophenylsulfonamido-1,2,3-trihydroxybenzene,

1,3-Dimethoxy-2-hydroxy-5-pentafluorophenylsulfonamidobenzene,

1,2-Dihydroxy-3-methoxy-5-pentafluorophenylsulfonamidobenzene,

5-Pentafluorophenylsulfonamido-1,2,3-trihydroxybenzene,

3-Hydroxy-5-methoxy-1-pentafluorophenylsulfonamidobenzene,

3,5-Dihydroxy-1-pentafluorophenylsulfonamidobenzene,

2-Fluoro-1-methoxy-4-(N-methylpentafluorophenylsulfonamido)benzene,

2-Bromo-1-methoxy-4-pentafluorophenylsulfonamidobenzene,

2-Chloro-1-methoxy-4-pentafluorophenylsulfonamidobenzene,

4-(N,N-Dimethylamino)-1-pentafluorophenylsulfonamidobenzene hydrochloride,

3,4-Difluoro-1-pentafluorophenylsulfonamidobenzene,

4-Trifluoromethoxy-1-pentafluorophenylsulfonamidobenzene,

2-Chloro-5-pentafluorophenylsulfonamidopyridine,

2-Hydroxy-1-methoxy-4-[N-(5-hydroxypentyl)pentafluorophenylsulfonamido]benzene,

4-(1,1-Dimethyl)ethoxy-1-pentafluorophenylsulfonamidobenzene,

2-Bromo-3-hydroxy-4-methoxy-1-pentafluorophenylsulfonamidobenzene,

2-Bromo-4-methoxy-5-hydroxy-1-pentafluorophenylsulfonamidobenzene,

1-Bromo-4-fluoro-5-methoxy-2-pentafluorophenylsulfonamidobenzene,

2-Hydroxy-1-methoxy-4-pentafluorophenylsulfonamidobenzene; sodium salt,

2-Hydroxy-1-methoxy-4-pentafluorophenylsulfonamidobenzene; potassium salt,

2-Fluoro-1-methoxy-4-pentafluorophenylsulfonamidobenzene; sodium salt,

2-Fluoro-1-methoxy-4-pentafluorophenylsulfonamidobenzene; potassium salt,

3-Chloro-1-pentafluorophenylsulfonamidobenzene,

4-Chloro-1-pentafluorophenylsulfonamidobenzene,

3-Nitro-1-pentafluorophenylsulfonamidobenzene,

4-Methoxy-1-pentafluorophenylsulfonamido-3-trifluoromethylbenzene,

4-Methoxy-1-(N-(2-propenyl)pentafluorophenylsulfonamido)benzene,

1-(N-(3-Butenyl)pentafluorophenylsulfonamido)-4-methoxybenzene,

4-Methoxy-1-(N-(4-pentenyl)pentafluorophenylsulfonamido)benzene,

1-(N-(2,3-Dihydroxypropyl)pentafluorophenylsulfonamido)-4-methoxybenzene,

1-(N-(3,4-Dihydroxybutyl)pentafluorophenylsulfonamido)-4-methoxybenzene,

1-(N-(4,5-Dihydroxypentyl)pentafluorophenylsulfonamido)-4-methoxybenzene,

1-(N-(4-hydroxybutyl)pentafluorophenylsulfonamido)-4-methoxybenzene,

4-Methoxy-1-(N-(5-hydroxypentyl)pentafluorophenylsulfonamido)benzene,

4-Methoxy-3-nitro-1-pentafluorophenylsulfonamidobenzene,

3-Amino-4-methoxy-1-pentafluorophenylsulfonamidobenzene,

4-Butoxy-1-pentafluorophenylsulfonamidobenzene,

1-Pentafluorophenylsulfonamido-4-phenoxybenzene,

4-Benzyloxy-1-pentafluorophenylsulfonamidobenzene,

4-Methylmercapto-1-pentafluorophenylsulfonamidobenzene,

2-Methoxy-1-pentafluorophenylsulfonamidobenzene,

4-Allyloxy-1-pentafluorophenylsulfonamidobenzene,

1-Pentafluorophenylsulfonamido-4-propoxybenzene,

4-(1-Methyl)ethoxy-1-pentafluorophenylsulfonamidobenzene,

1-Pentafluorophenylsulfonyloxybenzene,

1-Pentafluorophenylsulfonylindole,

1-Pentafluorophenylsulfonyl-1,2,3,4-tetrahydroquinoline,

2-Methoxy-5-pentafluorophenylsulfonamidopyridine,

2-Fluoro-1-methoxy-4-pentafluorophenylsulfinamide,

4-*tert*-Butoxy-1-pentafluorophenylsulfonamidobenzene, and

2-Anilino-3-pentafluorophenylsulfonamidopyridine.

48. The method of claim 47, wherein the compound is chosen from:

4-(N,N-Dimethylamino)-1-pentafluorophenylsulfonamidobenzene,

3-(N,N-Dimethylamino)-1-pentafluorophenylsulfonamidobenzene,

1,2-Ethylenedioxy-4-pentafluorophenylsulfonamidobenzene,

2-Hydroxy-1-methoxy-4-pentafluorophenylsulfonamidobenzene,

2-Fluoro-1-methoxy-4-pentafluorophenylsulfonamidobenzene,

4-Methoxy-1-pentafluorophenylsulfonamidobenzene,

3-Hydroxy-1-pentafluorophenylsulfonamidobenzene,

4-Hydroxy-1-pentafluorosulfonamidobenzene,

1,2-Dimethyl-4-pentafluorophenylsulfonamidobenzene,

5-Pentafluorophenylsulfonamidoindole,

4-(N,N-Dimethylamino)-1-(N-methylpentafluorophenylsulfonamido)benzene,

4-Ethoxy-1-pentafluorophenylsulfonamidobenzene,

3-Methoxy-1-pentafluorophenylsulfonamidobenzene,

2-Bromo-1-methoxy-4-pentafluorophenylsulfonamidobenzene,

2-Chloro-1-methoxy-4-pentafluorophenylsulfonamidobenzene,

2-Bromo-3-hydroxy-4-methoxy-1-pentafluorophenylsulfonamidobenzene,

2-Bromo-4-methoxy-5-hydroxy-1-pentafluorophenylsulfonamidobenzene,

1-Bromo-4-fluoro-5-methoxy-2-pentafluorophenylsulfonamidobenzene,

2-Hydroxy-1-methoxy-4-pentafluorophenylsulfonamidobenzene; monosodium salt,

2-Hydroxy-1-methoxy-4-pentafluorophenylsulfonamidobenzene: monopotassium salt,

2-Fluoro-1-methoxy-4-pentafluorophenylsulfonamidobenzene; sodium salt,

2-Fluoro-1-methoxy-4-pentafluorophenylsulfonamidobenzene; potassium salt,

4-Chloro-1-pentafluorophenylsulfonamidobenzene, and

3-Amino-4-methoxy-1-pentafluorophenylsulfonamidobenzene.

49. The method of claim 48, wherein the compound is:

2-Hydroxy-1-methoxy-4-pentafluorophenylsulfonamidobenzene,

2-Fluoro-1-methoxy-4-pentafluorophenylsulfonamidobenzene,

4-Methoxy-1-pentafluorophenylsulfonamidobenzene,

1,2-Dimethyl-4-pentafluorophenylsulfonamidobenzene,

5-Pentafluorophenylsulfonamidoindole,

4-Ethoxy-1-pentafluorophenylsulfonamidobenzene,

2-Bromo-1-methoxy-4-pentafluorophenylsulfonamidobenzene,

2-Chloro-1-methoxy-4-pentafluorophenylsulfonamidobenzene,

2-Bromo-3-hydroxy-4-methoxy-1-pentafluorophenylsulfonamidobenzene,

2-Bromo-4-methoxy-5-hydroxy-1-pentafluorophenylsulfonamidobenzene,

1-Bromo-4-fluoro-5-methoxy-2-pentafluorophenylsulfonamidobenzene,

2-Hydroxy-1-methoxy-4-pentafluorophenylsulfonamidobenzene: monosodium salt,

2-Hydroxy-1-methoxy-4-pentafluorophenylsulfonamidobenzene; monopotassium salt,

2-Fluoro-1-methoxy-4-pentafluorophenylsulfonamidobenzene; sodium salt.

2-Fluoro-1-methoxy-4-pentafluorophenylsulfonamidobenzene; potassium salt, or
3-Amino-4-methoxy-1-pentafluorophenylsulfonamidobenzene.

50. The method of claim 49, wherein the compound is
2-Hydroxy-1-methoxy-4-pentafluorophenylsulfonamidobenzene,
2-Hydroxy-1-methoxy-4-pentafluorophenylsulfonamidobenzene; monosodium salt, or
2-Hydroxy-1-methoxy-4-pentafluorophenylsulfonamidobenzene; monopotassium salt.

51. The method of claim 49, wherein the compound is
2-Fluoro-1-methoxy-4-pentafluorophenylsulfonamidobenzene.

52. The method of claim 49, wherein the compound is
2-Fluoro-1-methoxy-4-pentafluorophenylsulfonamidobenzene, sodium salt.

53. The method of claim 49, wherein the compound is
2-Fluoro-1-methoxy-4-pentafluorophenylsulfonamidobenzene, potassium salt.

54. The method of claim 43 in which the growth of a target cell is inhibited, which method comprises contacting said cell with an effective amount of a composition containing a compound of formula I.

55. The method of claim 43, wherein the proliferative disease state is cancer or a cancerous condition.

56. The method of claim 43, wherein the proliferative disease state is infection by a microorganism.

57. The method of claim 43, wherein the proliferative disease state is psoriasis.

58. The method of claim 43, wherein the proliferative disease state is vascular restenosis.

59. The method of claim 43, wherein the composition is administered orally.

60. The method of claim 43, wherein the compound is administered intravenously.

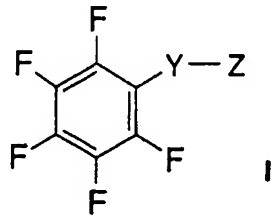
61. The method of claim 43 wherein the subject is administered intramuscularly.

62. The method of claim 43 wherein the composition is administered in combination with a therapeutically effective amount of an antineoproliferative, chemotherapeutic, or cytotoxic agent that is not represented by formula I.

63. The method of claim 43, wherein the compound is administered as a prodrug.

64. The method of claim 43, wherein the compound is conjugated to a targeting molecule which preferentially directs the compound to a targeted cell.

65. A compound having the formula I:



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or a pharmaceutically acceptable salt thereof, wherein:

Y is -S(O)- or -S(O_2)-; and

Z is NR^1R^2, wherein R^2 is an optionally substituted aryl or heteroaryl group, and R^1 is selected from

hydrogen,

substituted or unsubstituted (C1-C10)alkyl,

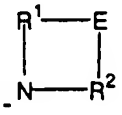
substituted or unsubstituted (C1-C10)alkoxy,

substituted or unsubstituted (C3-C6)alkenyl,

substituted or unsubstituted (C2-C6)heteroalkyl,

substituted or unsubstituted (C3-C6)heteroalkenyl,
substituted or unsubstituted (C3-C6)alkynyl,
substituted or unsubstituted (C3-C8)cycloalkyl,
substituted or unsubstituted (C5-C7)cycloalkenyl,
substituted or unsubstituted (C5-C7)cycloalkadienyl,
substituted or unsubstituted aryl,
substituted or unsubstituted aryloxy,
substituted or unsubstituted aryl-(C3-C8)cycloalkyl,
substituted or unsubstituted aryl-(C5-C7)cycloalkenyl,
substituted or unsubstituted aryloxy-(C3-C8)cycloalkyl,
substituted or unsubstituted aryl-(C1-C4)alkyl,
substituted or unsubstituted aryl-(C1-C4)alkoxy,
substituted or unsubstituted aryl-(C1-C4)heteroalkyl,
substituted or unsubstituted aryl-(C3-C6)alkenyl,
substituted or unsubstituted aryloxy-(C1-C4)alkyl,
substituted or unsubstituted aryloxy-(C2-C4)heteroalkyl,
substituted or unsubstituted heteroaryl,
substituted or unsubstituted heteroaryloxy,
substituted or unsubstituted heteroaryl-(C1-C4)alkyl,
substituted or unsubstituted heteroaryl-(C1-C4)alkoxy,
substituted or unsubstituted heteroaryl-(C1-C4)heteroalkyl,
substituted or unsubstituted heteroaryl-(C3-C6)alkenyl,
substituted or unsubstituted heteroaryloxy-(C1-C4)alkyl, and
substituted or unsubstituted heteroaryloxy-(C2-C4)heteroalkyl,

wherein R^1 and R^2 may be connected by a linking group E to give a substituent of the formula



wherein E represents a bond, (C1-C4) alkylene, or (C1-C4) heteroalkylene, and the ring formed by R^1, E, R^2 and the nitrogen contains no more than 8 atoms;

provided that:

in the case that Y is -S(O_2)-, and R^1 is hydrogen or methyl, then R^2 is substituted phenyl or heteroaryl group;

in the case that Y is -S(O_2)- and R^2 is a ring system chosen from 1-naphthyl, 5-quinolyl, or 4-pyridyl, then either R^1 is not hydrogen or R^2 is substituted by at least one substituent that is not hydrogen;

in the case that Y is -S(O_2)-, R^2 is phenyl, and R^1 is a propylene unit attaching the nitrogen of -NR^1R^2- to the 2- position of the phenyl ring in relation to the sulfonamido group to form a 1,2,3,4-tetrahydroquinoline system, and one or more of the remaining valences on the bicyclic system so formed is substituted with at least one substituent that is not hydrogen;

in the case that Y is -S(O_2)- and R^2 is phenyl substituted with 3-(1-hydroxyethyl), 3-dimethylamino, 4-dimethylamino, 4-phenyl, 3-hydroxy, 3-hydroxy-4-diethylaminomethyl, 3,4-methylenedioxy, 3,4-ethylenedioxy, 2-(1-pyrrolyl), or 2-methoxy-4-(1-morpholino), then either R^1 is not hydrogen or when R^1 is hydrogen, one or more of the remaining valences on the phenyl ring of R^2 is substituted with a substituent that is not hydrogen;

in the case that Y is -S(O_2)- and R^2 is 2-methylbenzothiazol-5-yl, 6-hydroxy-4-methyl-pyrimidin-2-yl, 3-carbomethoxypyrazin-2-yl, 5-carbomethoxypyrazin-2-yl, 4-carboethoxy-1-phenylpyrazol-5-yl, 3-methylpyrazol-5-yl, 4-chloro-2-methylthiopyrimidin-6-yl, 2-trifluoromethyl-1,3,4-thiadiazol-5-yl, 5,6,7,8-tetrahydro-2-naphthyl, 4-methylthiazol-2-yl, 6,7-dihydroindan-5-yl, 7-chloro-5-methyl-1,8-naphthyridin-2-yl, 5,7-dimethyl-1,8-naphthyridin-2-yl, or 3-cyanopyrazol-4-yl, then R^1 is a group other than hydrogen;

wherein said compound has pharmacological activity.

66. The compound of claim 65, wherein R^1 is hydrogen or lower alkyl, Y is -S(O_2)-, and there is no linking group E between R^1 and R^2.

67. The compound of claim 66, wherein R^1 is hydrogen or methyl and R^2 is substituted phenyl, wherein the substituents on R^2, ranging in number from one to four, are

independently chosen from lower alkyl, hydroxy, lower alkoxy, amino optionally substituted with one or two lower alkyls, optionally substituted arylamino, optionally substituted heteroarylamino, optionally substituted phenoxy, and halogen.

68. The compound of claim 67, wherein R^1 is hydrogen and R^2 is substituted phenyl, wherein the substituents on R^2 are independently chosen from amino, (lower)alkylamino, and di(lower)alkylamino, and are located at one or more of positions 3- and 4- of the phenyl ring, in relation to the sulfonamido group.

69. The compound of claim 68, wherein the compound is
4-(*N,N*-Diethylamino)-1-pentafluorophenylsulfonamidobenzene, or
4-Amino-1-pentafluorophenylsulfonamidobenzene.

70. The compound of claim 65, wherein R^1 is hydrogen, and R^2 is phenyl substituted at positions 3- and 4-, in relation to the sulfonamido group, with a divalent moiety that forms a 5- or 6- membered ring together with carbons 3- and 4- of the phenyl ring.

71. The compound of claim 70, wherein the divalent moiety is: -C=CNH-, or -C=NNH-.

72. The compound of claim 71, wherein the compound is 5-Pentafluorophenylsulfonamidoindazole or 5-Pentafluorophenylsulfonamidoindole.

73. The compound of claim 65, wherein R^1 is hydrogen, and the substituents on R^2 are independently selected from halogen, hydroxy, lower alkyl, lower alkoxy, amino, (lower)alkylamino, and di(lower)alkylamino.

74. The compound of claim 73, wherein the substituents on R^2 are independently selected from bromo, chloro, fluoro, hydroxy, methoxy, ethoxy, amino, or dimethylamino.

75. The compound of claim 74, wherein the substituents on R^2 are independently selected from bromo, chloro, fluoro, hydroxy, methoxy, and ethoxy.

76. The compound of claim 75, wherein the substituents on R^2 are at one or more of positions 3- and 4- of the phenyl ring, in relation to the sulfonamido group.

77. The compound of claim 76, wherein R^2 is monosubstituted phenyl.

78. The compound of claim 77, wherein the compound is
4-Methoxy-1-pentafluorophenylsulfonamidobenzene,
3-Hydroxy-1-pentafluorophenylsulfonamidobenzene,
4-Hydroxy-1-pentafluorophenylsulfonamidobenzene,
4-Ethoxy-1-pentafluorophenylsulfonamidobenzene,
3-Ethoxy-1-pentafluorophenylsulfonamidobenzene, or
3-Methoxy-1-pentafluorophenylsulfonamidobenzene.

79. The compound of claim 77, wherein the compound is
3-Chloro-1-pentafluorophenylsulfonamidobenzene, or
4-Chloro-1-pentafluorophenylsulfonamidobenzene.

80. The compound of claim 76, wherein R^2 is disubstituted phenyl.

81. The compound of claim 80, wherein the compound is
1,2-Dimethoxy-4-pentafluorophenylsulfonamidobenzene,
2-Hydroxy-1-methoxy-4-pentafluorophenylsulfonamidobenzene,
1,2-Dihydroxy-4-pentafluorophenylsulfonamidobenzene,
2-Hydroxy-1-methoxy-4-pentafluorophenylsulfonamidobenzene, monosodium salt, or
2-Hydroxy-1-methoxy-4-pentafluorophenylsulfonamidobenzene, monopotassium salt.

82. The compound of claim 80, wherein the compound is
2-Fluoro-1-methoxy-4-pentafluorophenylsulfonamidobenzene,
2-Bromo-1-methoxy-4-pentafluorophenylsulfonamidobenzene,
2-Chloro-1-methoxy-4-pentafluorophenylsulfonamidobenzene,

2-Fluoro-1-methoxy-4-pentafluorophenylsulfonamidobenzene, sodium salt, or
2-Fluoro-1-methoxy-4-pentafluorophenylsulfonamidobenzene, potassium salt.

83. The compound of claim 81, wherein the compound is
2-Hydroxy-1-methoxy-4-pentafluorophenylsulfonamidobenzene, or
2-Hydroxy-1-methoxy-4-pentafluorophenylsulfonamidobenzene, monosodium salt.

84. The compound of claim 82, wherein the compound is
2-Fluoro-1-methoxy-4-pentafluorophenylsulfonamidobenzene, or
2-Fluoro-1-methoxy-4-pentafluorophenylsulfonamidobenzene, sodium salt.

85. The compound of claim 84, wherein the compound is
2-Fluoro-1-methoxy-4-pentafluorophenylsulfonamidobenzene.

86. The compound of claim 84, wherein the compound is
2-Fluoro-1-methoxy-4-pentafluorophenylsulfonamidobenzene, sodium salt.

87. The compound of claim 76, wherein R^2 is trisubstituted phenyl.

88. The compound of claim 82, wherein the compound is
2-Bromo-1-methoxy-4-pentafluorophenylsulfonamidobenzene, or
2-Chloro-1-methoxy-4-pentafluorophenylsulfonamidobenzene.

89. The compound of claim 73, wherein the compound is
1,2-Dimethyl-4-pentafluorophenylsulfonamidobenzene.

90. The compound of claim 67, wherein the compound is
3-Phenoxy-1-pentafluorophenylsulfonamidobenzene.

91. The compound of claim 66, wherein R^2 is a phenyl ring substituted by a heterocyclic group at the 4- position, in relation to the sulfonamido group.

92. The compound of claim 78, wherein the compound is 4-Methoxy-1-pentafluorophenylsulfonamidobenzene.

93. The compound of claim 65, wherein R^1 and R^2 are covalently joined in a moiety that forms a 5- or 6- membered heterocyclic ring with the nitrogen atom of NR^1R^2.

94. The compound of claim 93, wherein R^1 is a -CH=CH- group linked to the 2- position of the R^2 phenyl group, in relation to the sulfonamido group, forming an optionally substituted indole.

95. The compound of claim 94, wherein the compound is 1-(Pentafluorophenylsulfonyl)indole.

96. The compound of claim 93, wherein R^1 is a $-(CH_2)_3-$ group linked to the 2- position of the R^2 phenyl group, in relation to the sulfonamido group, forming an optionally substituted 1,2,3,4-tetrahydroquinoline.

97. The compound of claim 65, wherein the compound is
2-Hydroxy-1-methoxy-4-[N-(5-hydroxypent-1-yl)pentafluorophenylsulfonamido]benzene.
4-Methoxy-1-[N-(2-propenyl)pentafluorophenylsulfonamido]benzene,
4-Methoxy-1-[N-(4-pentenyl)pentafluorophenylsulfonamido]benzene,
1-[N-(2,3-Dihydroxypropyl) pentafluorophenylsulfonamido]-4-methoxybenzene,
1-[N-(3,4-Dihydroxybutyl)pentafluorophenylsulfonamido]-4-methoxybenzene,
1-[N-(4,5-Dihydroxypentyl)pentafluorophenylsulfonamido]-4-methoxybenzene,
1-[N-(4-hydroxybutyl)pentafluorophenylsulfonamido]-4-methoxybenzene, or
4-Methoxy-1-[N-(5-hydroxypentyl)pentafluorophenylsulfonamido]benzene.

98. The composition of any of claim 1-42, or a method of any of claim 43-64, or a compound of any of claim 65-97, wherein the compound prevents cancerous cell growth.

99. A method for controlling cell proliferation, which method comprises covalently modifying selectively a ß tubulin.

100. The method of claim 99, which method comprises covalently modifying selectively Cys-239 of a ß tubulin.

101. A method for disrupting microtubule formation, which method comprises covalently modifying selectively a ß tubulin.

102. The method of claim 101, which method comprises covalently modifying selectively Cys-239 of a ß tubulin.

103. A natural ß tubulin covalently modified at selectively Cys-239.

104. A compound which covalently modifies selectively a ß tubulin.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US97/12720

A. CLASSIFICATION OF SUBJECT MATTER

IPC(6) :Please See Extra Sheet.
US CL :Please See Extra Sheet.
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : Please See Extra Sheet.

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

None

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

CAS ONLINE

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	Chem. abstr., Vol. 118, No. 7, 15 February 1993 (Columbus, OH, USA), page 810, column 2, the abstract No. 59373g, FIELDING et al. 'Synthesis and Reactions of 4-Sulfo-2,3,5,6-tetrafluorobenzoic Acid.' J. Fluorine Chem.. 1992, 59(1), 15-31 (Eng), see entire abstract.	1-3, 8, 98, 104
Y	US 1,955,207 A (STOTTER et al.) 17 April 1934, see entire document.	1-4, 8, 9, 12-33, 35, 42, 65-67, 70, 73-90, 92, 97, 98, 104

[X] Further documents are listed in the continuation of Box C. [ ] See patent family annex.

*	Special categories of cited documents:	"T"	later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"A"	document defining the general state of the art which is not considered to be of particular relevance	"X"	document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"E"	earlier document published on or after the international filing date	"Y"	document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"L"	document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"&"	document member of the same patent family
"O"	document referring to an oral disclosure, use, exhibition or other means		
"P"	document published prior to the international filing date but later than the priority date claimed		

Date of the actual completion of the international search 16 DECEMBER 1997	Date of mailing of the international search report 14 JAN 1998
Name and mailing address of the ISA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. (703) 305-3230	Authorized officer Peter G. O'Sullivan Telephone No. (703) 308-1235

Form PCT/ISA/210 (second sheet)(July 1992)*

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US97/12720

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US 2,402,623 A (HESTER, W.F.) 25 June 1946, see entire document.	1-4, 8, 9, 12-33, 35, 42, 65-67, 70, 73-90, 92, 97, 98, 104
Y	US 3,034,955 A (FRICK et al.) 15 May 1962, see entire document.	1-4, 8, 9, 12-33, 35, 42, 65-67, 70, 73-90, 92, 97, 98, 104
X	Chem. abstr., Vol. 121, No. 19, 07 November 1994 (Columbus. OH, USA), pages 486 and 487, bridging paragraph, the abstract No. 224943q, RAIBEKAS et al. 'Affinity Probing of Flavin Binding Sites. 2. Identification of Reactive Cysteine in the Flavin Domain of Escherichia coli DNA Photolyase.' Biochemistry. 1994, 33(42), 12656-12664 (Eng), see entire abstract.	99-104
A	US 5,250,549 A (YOSHINO et al.) 05 October 1993, see entire document.	1-104

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US97/12720

A. CLASSIFICATION OF SUBJECT MATTER:
IPC (6):

A61K 31/165, 31/255, 31/35, 31/36, 31/40, 31/44, 31/47, 31/50, 31/535; C07C 311/21, 313/04, 313/06; C07D 209/08, 213/76, 215/38, 231/56, 317/66, 319/18; C07K 14/00

A. CLASSIFICATION OF SUBJECT MATTER:
US CL :

514/231.2, 311, 353, 406, 415, 452, 466, 516, 604, 608; 530/402, 408; 544/159; 546/164, 307; 548/362.5, 516; 549/366, 439; 558/58; 564/90, 92, 101

B. FIELDS SEARCHED
Minimum documentation searched
Classification System: U.S.

514/231.2, 311, 353, 406, 415, 452, 466, 516, 604, 608; 530/402, 408; 544/159; 546/164, 307; 548/362.5, 516; 549/366, 439; 558/58; 564/90, 92, 101